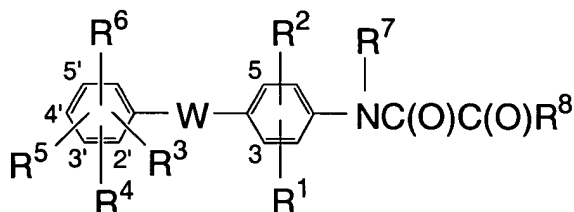


CLAIMS

1. A method for increasing the rate of nail growth in a mammal which comprises the local administration of a thyromimetic compound to the mammal.
2. A method of claim 1 wherein the thyromimetic compound is administered to the nail and/or immediately surround tissue.
3. A method of claim 1 wherein the thyromimetic compound is administered topically.
4. A method for increasing the rate of nail growth in a mammal which comprises the administration to the mammal of an effective amount of a compound of the formula



a prodrug thereof, a geometric or optical isomer thereof, or a pharmaceutically acceptable salt of said compound, said prodrug, or said isomer, wherein:

- R^1 , R^2 and R^3 are each independently hydrogen, halogen, C_{1-6} alkyl, trifluoromethyl, -CN, -OCF₃ or -OC₁₋₆ alkyl;
- R^4 is hydrogen, C_{1-12} alkyl optionally substituted with one to three substituents independently selected from Group Z, C_{2-12} alkenyl, halogen, -CN, aryl, heteroaryl, C_{3-10} cycloalkyl, heterocycloalkyl, -S(O)₂NR⁹R¹⁰, -C(O)NR⁹R¹⁰, -(C₁₋₆ alkyl)-NR⁹R¹⁰, -NR⁹C(O)R¹⁰, -NR⁹C(O)NR⁹R¹⁰, -NR⁹S(O)₂R¹⁰, -(C₁₋₆ alkyl)-OR¹¹, -OR¹¹ or -S(O)_aR¹², provided that, where R^5 is not fluoro, R^4 is -S(O)₂NR⁹R¹⁰, -C(O)NR⁹R¹⁰, -(C₁₋₆ alkyl)-NR⁹R¹⁰, -NR⁹C(O)R¹⁰, -NR⁹C(O)NR⁹R¹⁰, -NR⁹S(O)₂R¹⁰, -(C₁₋₆ alkyl)-OR¹¹, -OR¹¹ or -S(O)_aR¹²;
- or R^3 and R^4 may be taken together to form a carbocyclic ring A of the formula -(CH₂)_b- or a heterocyclic ring A selected from the group consisting of -Q-(CH₂)_c- and -(CH₂)_j-Q-(CH₂)_k- wherein Q is O, S or NR¹⁷, wherein said carbocyclic ring A and said heterocyclic ring A are each independently optionally substituted with one or more substituents independently selected from C₁₋₄ alkyl, halide or oxo;
- R^5 is fluoro, hydroxy, C₁₋₄ alkoxy or OC(O)R⁹;

or R⁴ and R⁵ may be taken together to form a heterocyclic ring B selected from the group consisting of -CR⁹=CR¹⁰-NH-, -N=CR⁹-NH-, -CR⁹=CH-O- and -CR⁹=CH-S-;

R⁶ is hydrogen, halogen, C₁₋₄ alkyl or trifluoromethyl;

5 R⁷ is hydrogen or C₁₋₆ alkyl;

R⁸ is -OR⁹ or -NR¹⁹R²⁰;

R⁹ and R¹⁰ for each occurrence are independently (A) hydrogen, (B) C₁₋₁₂ alkyl optionally substituted with one or more substituents independently selected from Group V, (C) C₂₋₁₂ alkenyl, (D) C₃₋₁₀ cycloalkyl optionally substituted with one or more substituents independently selected from C₁₋₆ alkyl, C₂₋₅ alkynyl, C₃₋₁₀ cycloalkyl, -CN, -NR¹³R¹⁴, oxo, -OR¹⁸, -COOR¹⁸ or aryl optionally substituted with X and Y, (E) aryl optionally substituted with X and Y, or (F) het optionally substituted with X and Y;

or R⁹ and R¹⁰ for any occurrence may be taken together to form a heterocyclic ring C optionally further containing a second heterogroup selected from the group consisting of -O-, -NR¹³- and -S-, and optionally further substituted with one or more substituents independently selected from C₁₋₅ alkyl, oxo, -NR¹³R¹⁴, -OR¹⁸, -C(O)₂R¹⁸, -CN, -C(O) R⁹, aryl optionally substituted with X and Y, het optionally substituted with X and Y, C₅₋₆ spirocycloalkyl, and a carbocyclic ring B selected from the group consisting of 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated carbocyclic rings, and including any bicyclic group in which said carbocyclic ring B is fused to a carbocyclic ring C selected from the group consisting of 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated carbocyclic rings;

25 R¹¹ is C₁₋₁₂ alkyl optionally substituted with one or more substituents independently selected from Group V, C₂₋₁₂ alkenyl, C₃₋₁₀ cycloalkyl, trifluoromethyl, difluoromethyl, monofluoromethyl, aryl optionally substituted with X and Y, het optionally substituted with X and Y, -C(O)NR⁹R¹⁰ or -C(O)R⁹;

R¹² is C₁₋₁₂ alkyl optionally substituted with one or more substituents independently selected from Group V, C₂₋₁₂ alkenyl, C₃₋₁₀ cycloalkyl, aryl optionally substituted with X and Y, or het optionally substituted with X and Y;

30 R¹³ and R¹⁴ for each occurrence are independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, -(C₁₋₆ alkyl)-C₁₋₆ alkoxy, aryl optionally substituted with X and Y, het optionally substituted with X and Y, -(C₁₋₄ alkyl)-aryl optionally substituted with X

and Y, -(C₁₋₄ alkyl)-heterocycle optionally substituted with X and Y, -(C₁₋₄ alkyl)-hydroxy, -(C₁₋₄ alkyl)-halo, -(C₁₋₄ alkyl)-poly-halo, -(C₁₋₄ alkyl)-CONR¹⁵R¹⁶ or C₃₋₁₀ cycloalkyl;

R¹⁵ and R¹⁶ for each occurrence are independently hydrogen, C₁₋₆ alkyl, C₃₋₁₀ cycloalkyl or aryl optionally substituted with X and Y;

R¹⁷ is hydrogen, C₁₋₆ alkyl, -COR⁹ or -SO₂R⁹ ;

R¹⁸ is hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, -(C₁₋₆ alkyl)-C₁₋₆ alkoxy, aryl optionally substituted with X and Y, het optionally substituted with X and Y, -(C₁₋₄ alkyl)-aryl optionally substituted with X and Y, -(C₁₋₄ alkyl)-heterocycle optionally substituted with X and Y, -(C₁₋₄ alkyl)-hydroxy, -(C₁₋₄ alkyl)-halo, -(C₁₋₄ alkyl)-poly-halo, -(C₁₋₄ alkyl)-CONR¹⁵R¹⁶, -(C₁₋₄ alkyl)-(C₁₋₄ alkoxy) or C₃₋₁₀ cycloalkyl;

R¹⁹ is hydrogen or C₁₋₆ alkyl;

R²⁰ is hydrogen or C₁₋₆ alkyl;

W is O, S(O)_d, CH₂ or NR⁹ ;

Group Z is C₂₋₆ alkenyl, C₂₋₆ alkynyl, halogen, -CF₃, -OCF₃, hydroxy, oxo, -CN, aryl, heteroaryl, C₃₋₁₀ cycloalkyl, heterocycloalkyl, -S(O)_aR¹², -S(O)₂NR⁹R¹⁰, -C(O)R⁹R¹⁰, and -NR⁹R¹⁰;

Group V is halogen, -NR¹³R¹⁴, -OCF₃, -OR⁹, oxo, trifluoromethyl, -CN, C₃₋₁₀ cycloalkyl, aryl optionally substituted with X and Y, and het optionally substituted with X and Y;

het for each occurrence is a heterocyclic ring D selected from the group consisting of 4-, 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated, heterocyclic rings containing from one to four heteroatoms independently selected from the group consisting of N, O and S, and including any bicyclic group in which said heterocyclic ring D is fused to a benzene ring or a heterocyclic ring E selected from the group consisting of 4-, 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated, heterocyclic rings containing from one to four heteroatoms independently selected from the group consisting of N, O and S;

X and Y for each occurrence are independently (A) hydrogen, (B) halogen, (C) trifluoromethyl, (D) -OCF₃, (E) -CN, (F) C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, -OCF₃, -CF₃ and phenyl, (G) C₁₋₆ alkoxy, (H) aryl optionally substituted with one or more substituents independently selected from the group consisting of halogen,

-OCF₃, -CF₃, C₁₋₄ alkyl and C₁₋₄ alkoxy, (I) -C(O)₂R¹³, (J) -C(O)NR¹³R¹⁴, (K) -C(O)R¹³, (L) -NR¹³C(O)NR¹³R¹⁴ and (M) -NR¹³C(O)R¹⁴ ;

or X and Y for any occurrence in the same variable may be taken together to form (a) a carbocyclic ring D of the formula -(CH₂)_e- or (b) a heterocyclic ring F
5 selected from the group consisting of -O(CH₂)_iO-, (CH₂)_gNH- and -CH=CHNH- ;

a and d are each independently 0, 1 or 2;

b is 3, 4, 5, 6 or 7;

c, f, g, j and k are each independently 2, 3, 4, 5 or 6; and

e is 3, 4, 5, 6 or 7.

10 5. A method of claim 4 wherein the compound is selected from the group consisting of:

N-[3-chloro-4-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-oxamic acid;

15 N-[4-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;

N-{4-[3-(cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-oxamic acid;

N-{3-chloro-4-[3-(cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-oxamic acid;

20 N-[4-(7-hydroxy-indan-4-yloxy)-3,5-dimethyl-phenyl]-oxamic acid;

N-{3,5-dichloro-4-[3-(cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-phenyl}-oxamic acid;

N-[3,5-dichloro-4-(3-cyclopentanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;

25 N-[3,5-dichloro-4-(3-cyclopropylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;

N-[3,5-dichloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;

30 N-[4-(3-cyclopropylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;

N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-oxamic acid;

N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;

N-[4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;

N-[3-chloro-4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-oxamic acid;

5 N-[3,5-dichloro-4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;

N-[4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;

10 N-[3-chloro-4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-oxamic acid;

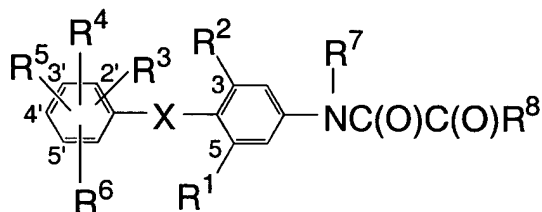
N-[3,5-dichloro-4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;

N-[3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl]-oxamic acid;

15 N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-oxamic acid; and

N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-oxamic acid.

20 6. A method for increasing the rate of nail growth in a mammal which comprises the administration to the mammal of an effective amount of a compound of the formula



25 a prodrug thereof, a geometric or optical isomer thereof, or a pharmaceutically acceptable salt of said compound, said prodrug, or said isomer, wherein:

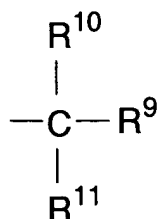
R¹ and R² are independently halogen, C₁₋₈ alkyl, -CN or C₁₋₈ perfluoroalkyl; provided that at least one of R¹ and R² is -CN;

R³ is hydrogen or C₁₋₈ alkyl;

30 R⁴ is halogen, C₁₋₈ perfluoroalkyl, C₁₋₈ alkyl, C₁₋₈ alkanoyl, hydroxy-(C₁₋₈ alkyl), aryl optionally substituted with Y and Z, aryl-(C₁₋₈ alkyl), carbocyclic aroyl

optionally substituted with Y and Z, C₃₋₁₀ cycloalkyl optionally substituted with Y and Z, or C₃₋₁₀ cycloalkyl-(C₁₋₈ alkyl);

or R⁴ is the radical



- 5 wherein: R⁹ is hydrogen, C₁₋₈ alkyl, aryl optionally substituted with Y and Z, aryl-(C₁₋₈ alkyl), C₃₋₁₀ cycloalkyl optionally substituted with Y and Z, or C₃₋₁₀ cycloalkyl-(C₁₋₈ alkyl); R¹⁰ is -OR¹⁴; R¹¹ is hydrogen or C₁₋₈ alkyl; or R¹⁰ and R¹¹ may be taken together with the carbon atom to which they are attached to form a carbonyl group;

R⁵ is hydroxy, esterified hydroxy or etherified hydroxy;

- 10 R⁶ is hydrogen, halogen, C₁₋₈ alkyl or C₁₋₈ perfluoroalkyl;

R⁷ is hydrogen, C₁₋₈ alkyl or C₁₋₈ perfluoroalkyl;

R⁸ is -OR¹² or -NR¹²R¹³;

R¹² and R¹³ are each independently hydrogen or C₁₋₈ alkyl;

R¹⁴ is hydrogen, C₁₋₈ alkyl or C₁₋₈ acyl;

- 15 X is O, S(O)_a, C=O or NR¹⁵;

a is 0, 1 or 2;

R¹⁵ is hydrogen or C₁₋₈ alkyl;

- Y and Z for each occurrence are independently (a) hydrogen, (b) halogen, (c) trifluoromethyl, (d) -OCF₃, (e) -CN, (f) C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, -OCF₃, -CF₃ and phenyl, (g) C₁₋₆ alkoxy, (h) aryl optionally substituted with one or more substituents independently selected from the group consisting of halogen, -OCF₃, -CF₃, C₁₋₄ alkyl and C₁₋₄ alkoxy, (i) -C(O)₂R¹⁶, (j) -C(O)NR¹⁶R¹⁷, (k) -C(O)R¹⁶, (l) -NR¹⁶C(O)NR¹⁶R¹⁷ or (m) -NR¹⁶C(O)R¹⁷; or Y and Z for any occurrence may be taken together to form (a) a carbocycle of the formula -(CH₂)_b, or (b) a heterocycle selected from the group consisting of -O(CH₂)_cO-, -(CH₂)_dNH- and -CH=CHNH-;

b is 3, 4, 5, 6 or 7;

c and d are each independently 2, 3, 4, 5 or 6;

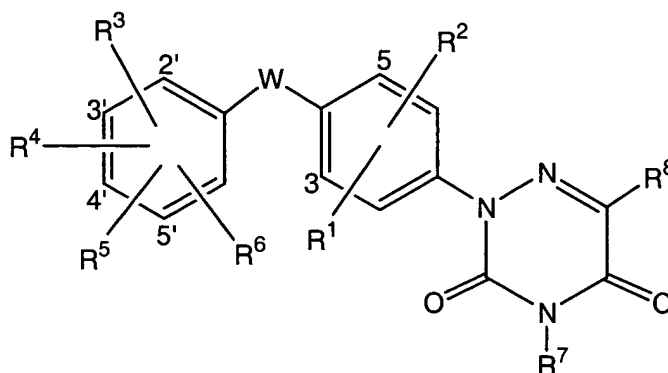
- 30 R¹⁶ and R¹⁷ for each occurrence are independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, -(C₁₋₆ alkyl)-C₁₋₆ alkoxy, aryl optionally substituted with X and Y, het

optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -aryl optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -heterocycle optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -hydroxy, $-(C_{1-4} \text{ alkyl})$ -halo, $-(C_{1-4} \text{ alkyl})$ -poly-halo, $-(C_{1-4} \text{ alkyl})$ -CONR¹⁸R¹⁹ or C₃₋₁₀ cycloalkyl;

- 5 het for each occurrence is a heterocyclic ring selected from the group consisting of 4-, 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated, heterocyclic rings containing from one to four heteroatoms independently selected from the group consisting of N, O and S, and including any bicyclic group in which said heterocyclic ring is fused to a benzene ring or a
10 heterocyclic ring selected from the group consisting of 4-, 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated, heterocyclic rings containing from one to four heteroatoms independently selected from the group consisting of N, O and S; and

- R¹⁸ and R¹⁹ for each occurrence are independently hydrogen, C₁₋₆ alkyl, C₃₋₁₀ cycloalkyl or aryl optionally substituted with Y and Z.
15

7. A method for increasing the rate of nail growth in a mammal which comprises the administration to the mammal of an effective amount of a compound of the formula



- 20 an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug; wherein W is (a) -O-, (b) -S(O)_m-, (c) -NR³⁰-, (d) -C(O)-, (e) -HC=CH-, (f) -CH₂-, (g) -CHF-, (h) -CF₂- or (i) -CH(OH)-;

- R¹ and R² are independently (a) hydrogen, (b) halogen, (c) $-(C_1-C_6) \text{ alkyl}$, (d) -CN, (e) -OR¹² or (f) -trifluoromethyl;
25

 R³ is (a) hydrogen, (b) halogen, (c) $-(C_1-C_6) \text{ alkyl}$ optionally substituted with one to three substituents independently selected from the group consisting of

halogen, $-\text{OCF}_3$ and $-\text{CF}_3$, (d) $-\text{CN}$, (e) $-\text{OR}^{12}$, (f) $-\text{trifluoromethyl}$, (g) $-\text{NO}_2$, (h) $-\text{SO}_2-\text{R}^{13}$, (i) $-\text{C}(\text{O})_2\text{R}^9$, (j) $-\text{C}(\text{O})\text{NR}^{19}\text{R}^{20}$, (k) $-\text{C}(\text{O})\text{R}^{16}$, (l) $-\text{NR}^{21}\text{C}(\text{O})-\text{NR}^{21}\text{R}^{22}$, (m) $-\text{NR}^{19}-\text{C}(\text{O})\text{R}^{20}$ or (n) $-\text{NR}^{17}\text{R}^{18}$;

R^4 is (a) $-\text{C}(\text{R}^{14})(\text{R}^{15})(\text{R}^{16})$, (b) $-(\text{C}_0-\text{C}_3)\text{alkyl}-\text{NR}^{17}\text{R}^{18}$, (c) $-\text{C}(\text{O})\text{NR}^{19}\text{R}^{20}$, (d) $-\text{NR}^{19}-\text{C}(\text{O})-\text{R}^{20}$, (e) $-(\text{C}_0-\text{C}_3)\text{alkyl}-\text{NR}^{21}-\text{C}(\text{O})-\text{NR}^{21}\text{R}^{22}$, (f) $-\text{S}(\text{O})_m-\text{R}^{22}$, (g) $-\text{S}(\text{O})_2-\text{NR}^{21}\text{R}^{22}$, (h) $-\text{NR}^{21}-\text{S}(\text{O})_2-\text{R}^{22}$, (i) $-\text{aryl}$, (j) $-\text{het}$, (k) $-\text{OR}^{33}$ or (l) halogen; provided that in substituents (f) and (h), R^{22} is other than $-\text{OR}^{34}$; and provided that when substituent (b) is $-(\text{C}_0)\text{alkyl}-\text{NR}^{17}\text{R}^{18}$, R^{18} is other than $-\text{C}(\text{O})-\text{R}^{28}$ or $-\text{S}(\text{O})_2-\text{R}^{29}$;

or R^3 and R^4 may be taken together to form a carbocyclic ring of Formula -
 10 $(\text{CH}_2)_b-$ or a heterocyclic ring selected from the group consisting of $-\text{Q}-(\text{CH}_2)_c-$ and $-(\text{CH}_2)_j-\text{Q}-(\text{CH}_2)_k-$ wherein Q is O, S or NR^{25} ; wherein said carbocyclic ring is optionally substituted with one or more substituents independently selected from Group V; and wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from Group Z;

15 R^5 is $-\text{OR}^{23}$;

or R^4 and R^5 may be taken together to form a heterocyclic ring selected from the group consisting of $-\text{CR}^{31}=\text{CR}^{32}-\text{NH}-$, $-\text{N}=\text{CR}^{31}-\text{NH}-$, $-\text{CR}^{31}=\text{CR}^{32}-\text{O}-$ and $-\text{CR}^{31}=\text{CR}^{32}-\text{S}-$;

R^6 is (a) hydrogen, (b) halogen, (c) $-(\text{C}_1-\text{C}_6)\text{alkyl}$ optionally substituted with
 20 one to three substituents independently selected from the group consisting of halogen, $-\text{OCF}_3$ and $-\text{CF}_3$, (d) $-\text{CN}$, (e) $-\text{OR}^{12}$, (f) $-\text{trifluoromethyl}$, (g) $-\text{NO}_2$, (h) $-\text{SO}_2-\text{R}^{13}$, (i) $-\text{C}(\text{O})_2\text{R}^9$, (j) $-\text{C}(\text{O})\text{NR}^{19}\text{R}^{20}$, (k) $-\text{C}(\text{O})\text{R}^{16}$, (l) $-\text{NR}^{21}\text{C}(\text{O})\text{NR}^{21}\text{R}^{22}$, (m) $-\text{NR}^{19}-\text{C}(\text{O})\text{R}^{20}$ or (n) $-\text{NR}^{17}\text{R}^{18}$;

R^7 is (a) hydrogen, (b) $-(\text{C}_1-\text{C}_4)\text{alkyl}$ wherein each carbon atom is optionally
 25 substituted with 1 to 3 halo atoms or (c) $-(\text{CH}_2)_n\text{COOR}^9$;

R^8 is (a) hydrogen, (b) $-(\text{C}_1-\text{C}_6)\text{alkyl}$, (c) $-\text{C}(\text{O})-\text{OR}^9$, (d) $-\text{C}(\text{O})\text{NR}^{10}\text{R}^{11}$ or (e) $-\text{CN}$; provided that in substituent (c), R^9 is other than methyl or ethyl; and provided that in substituent (d), R^{10} and R^{11} are not both hydrogen;

R^9 is (a) $-(\text{C}_1-\text{C}_{12})\text{alkyl}$ optionally substituted with one or more substituents
 30 independently selected from Group V, (b) $-(\text{C}_2-\text{C}_{12})\text{alkenyl}$ optionally substituted with phenyl, (c) $-(\text{C}_2-\text{C}_{12})\text{dialkenyl}$, (d) $-(\text{C}_3-\text{C}_{10})\text{cycloalkyl}$, (e) $-\text{aryl}$ or (f) $-\text{het}$;

R^{10} and R^{11} are independently (a) hydrogen, (b) $-(\text{C}_1-\text{C}_{12})\text{alkyl}$ optionally substituted with one or more substituents independently selected from Group V, (c)

-(C₃-C₁₀)cycloalkyl optionally substituted with one or more substituents

independently selected from Group V, (d) -(C₂-C₁₂)alkenyl or (e) -het;

or R¹⁰ and R¹¹ for any occurrence may be taken together with the nitrogen atom to which are they attached to form het;

5 R¹² is (a) hydrogen or (b) -(C₁-C₆)alkyl wherein each carbon atom is optionally substituted with 1 to 3 fluoro atoms;

R¹³ is (a) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (b) -(C₂-C₁₂)alkenyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -NR¹⁷R¹⁸, (e) -aryl or (f) -het;

10 R¹⁴ is (a) hydrogen, (b) -(C₁-C₆)alkyl or (c) -O-R³⁴;

R¹⁵ is (a) hydrogen or (b) -(C₁-C₆)alkyl;

or R¹⁴ and R¹⁵ are taken together with the carbon atom to which they are attached to form a carbonyl group;

15 R¹⁶ is (a) hydrogen, (b) -(C₁-C₆)alkyl wherein each carbon atom is optionally substituted with 1 to 3 fluoro atoms, (c) -(C₀-C₆)alkyl-(C₃-C₁₀)cycloalkyl, (d) -(C₀-C₆)alkyl-aryl or (e) -(C₀-C₆)alkyl-het;

R¹⁷ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -aryl, (d) -het, (e) -OR³⁴ or (f) -(C₃-C₁₀)cycloalkyl;

20 R¹⁸ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -aryl, (d) -het, (e) -C(O)-R²⁸, (f) -S(O)₂-R²⁹, (g) -OR³⁴ or (h) -(C₃-C₁₀)cycloalkyl;

or R¹⁷ and R¹⁸ for any occurrence are taken together with the nitrogen atom to which they are attached to form het;

25 R¹⁹ and R²⁰ for each occurrence are independently (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₀-C₆)alkyl-aryl, (d) -(C₀-C₆)alkyl-het, (e) -C(O)-NR²⁶R²⁷, (f) -C(O)-R²⁸, (g) -S(O)₂-R²⁹, (h) -OR³⁴ or (i) -(C₃-C₁₀)cycloalkyl;

30 or R¹⁹ and R²⁰ for any occurrence are taken together with the nitrogen atom to which they are attached to form het;

R²¹ and R²² for each occurrence are independently

(a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one to three substituents independently selected from Group V, (c) -aryl, (d) -het, (e) -(C₃-C₁₀)cycloalkyl or

(f) -OR³⁴;

or R²¹ and R²² are taken together with the nitrogen atom to which they are attached to form het;

R²³ is (a) hydrogen, (b) -(C₁-C₄)alkyl optionally substituted with one or more substituents independently selected from Group V or (c) -C(O)-R²⁴;

R²⁴ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R²⁵ for each occurrence is independently (a) hydrogen, (b) -(C₁-C₆)alkyl, (c) -COR²⁹ or (d) -SO₂R²⁹;

R²⁶ and R²⁷ for each occurrence are independently (a) hydrogen, (b) -(C₁-C₆)alkyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -(C₀-C₆)alkyl-aryl, or (e) -(C₀-C₆)alkyl-het,

R²⁸ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R²⁹ is (a) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (b) -(C₂-C₁₂)alkenyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -aryl or (e) -het;

R³⁰ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₁-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -C(O)-R³¹ or (f) -S(O)_m-R³²;

R³¹ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl, (f) -het or (g) -OR³⁴;

R³² is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R³³ is (a) -(C₀-C₆)alkyl-aryl, (b) -(C₀-C₆)alkyl-het, (c) -(C₇-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (d) -(C₁-C₆)alkyl wherein at least one carbon atom is substituted with 1 to 3 fluoro atoms, (e) -(C₂-C₁₂)alkenyl or (f) -(C₃-C₁₀)cycloalkyl;

R³⁴ is (a) -aryl, (b) -het, (c) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (d) -(C₂-C₁₂)alkenyl or (e) -(C₃-C₁₀)cycloalkyl;

5 -(C₃-C₁₀)cycloalkyl for each occurrence is a fully or partially saturated mono-, bi- or tricyclic ring containing three to ten carbon atoms; wherein in the bicyclic ring, a monocyclic cycloalkyl ring is spiro fused to another cycloalkyl ring or is fused via two carbon atoms to a benzene ring or another cycloalkyl ring; and wherein in the tricyclic ring, a bicyclic ring is spiro fused to a cycloalkyl ring or is fused via two atoms to a benzene ring or another cycloalkyl ring;

10 said -(C₃-C₁₀)cycloalkyl optionally contains one to three bridging atoms independently selected from carbon, oxygen, sulfur and nitrogen; said bridging atoms are attached to two carbon atoms in the ring; and said bridging atoms are optionally substituted with one to three groups independently selected from -(C₁-C₆)alkyl and hydroxy;

15 said cycloalkyl ring is optionally substituted on one ring if the moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with one or more substituents independently selected from Group V;

20 Group V is (a) -(C₁-C₆)alkyl optionally substituted with one or two hydroxy, (b) -(C₂-C₅)alkynyl, (c) -halogen, (d) -NR³⁵R³⁶, (e) -NO₂, (f) -OCF₃, (g) -OR³⁷, (h) -SR³⁷, (i) -oxo, (j) -trifluoromethyl, (k) -CN, (l) -C(O)NR³⁵-OH, (m) -COOR³⁵, (n) -O-C(O)-(C₁-C₆)alkyl, (o) -(C₃-C₁₀)cycloalkyl optionally substituted with CN, (p) -(C₀-C₆)alkyl-aryl, (q) -(C₀-C₆)alkyl-het, (r) -C(O)-(C₁-C₆)alkyl or (s) -C(O)-aryl;

25 R³⁵ and R³⁶ for each occurrence are independently (a) hydrogen, (b) -(C₁-C₆)alkyl or (c) -(C₀-C₆)alkyl-aryl;

 R³⁷ is (a) hydrogen, (b) -(C₁-C₆)alkyl optionally substituted with one or more halo, hydroxy or methoxy, (c) -(C₀-C₆)alkyl-aryl or (d) -(C₀-C₆)alkyl-het;

30 aryl is (a) phenyl optionally substituted with one or more substituents independently selected from Group Z; (b) naphthyl optionally substituted with one or more substituents independently selected from Group Z or (c) biphenyl optionally substituted with one or more substituents independently selected from Group Z;

 het for each occurrence is a 4-, 5-, 6-, 7- and 8-membered fully saturated, partially saturated or fully unsaturated mono-, bi- or tricyclic heterocyclic ring containing from one to four heteroatoms independently selected from the group

consisting of oxygen, sulfur and nitrogen; wherein in the bicyclic ring, a monocyclic heterocyclic ring is spiro fused to a $-(C_3-C_8)$ cycloalkyl ring or to another heterocyclic ring which is fully or partially saturated; or is fused via two atoms to a benzene ring, a $-(C_3-C_8)$ cycloalkyl ring or another heterocyclic ring; and wherein in the tricyclic
5 ring, a bicyclic ring is spiro fused to a $-(C_3-C_8)$ cycloalkyl ring or to another heterocyclic ring which is fully or partially saturated; or is fused via two atoms to a benzene ring, a (C_3-C_6) cycloalkyl ring, or another heterocyclic ring;

said het optionally contains one to three bridging atoms independently selected from oxygen, sulfur and nitrogen; said bridging atoms are attached to two
10 other atoms in the ring; and said bridging atoms are optionally substituted with one to three groups independently selected from $-(C_1-C_6)$ alkyl and hydroxy;

said het optionally has one or two oxo groups substituted on carbon or one or two oxo groups substituted on sulfur;

said het is optionally substituted on carbon or nitrogen, on one ring if the
15 moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with one or more substituents independently selected from Group Z;

Group Z for each occurrence is independently (a) hydrogen, (b) halogen, (c) trifluoromethyl, (d) hydroxy, (e) $-OCF_3$, (f) $-CN$, (g) $-NO_2$, (h) $-(C_1-C_6)$ alkyl
20 optionally substituted with one or more substituents independently selected from the group consisting of hydroxy, halogen, $-OCF_3$ and $-CF_3$, (i) $-(C_2-C_6)$ alkenyl optionally substituted with phenyl, (j) $-(C_2-C_5)$ alkynyl, (k) $-(C_1-C_6)$ alkoxy, (l) $-(C_0-C_6)$ alkyl-phenyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, $-OCF_3$, $-CF_3$, $-(C_1-C_4)$ alkyl, $-(C_1-C_4)$ alkoxy and $-C(O)CH_3$, (m) $-(C_0-C_6)$ alkyl-naphthyl optionally substituted with one
25 or more substituents independently selected from the group consisting of halogen, $-OCF_3$, $-CF_3$, $-(C_1-C_4)$ alkyl, $-(C_1-C_4)$ alkoxy and $-C(O)CH_3$, (n) $-C(O)_2R^{35}$, (o) $-(C_0-C_6)$ alkyl- $C(O)NR^{35}R^{36}$, (p) $-(C_0-C_6)$ alkyl- $C(O)R^{38}$, (q) $-NR^{35}R^{36}$, (r) $-NR^{35}-C(O)NR^{35}R^{36}$, (s) $-NR^{35}-C(O)R^{36}$, (t) $-OR^{37}$, (u) $-SR^{37}$, (v) $-(C_3-C_{10})$ cycloalkyl, (w) $-(C_0-C_6)$ alkyl-pyridinyl optionally substituted with one or more $-(C_1-C_6)$ alkyl which is
30 optionally substituted with one or more substituents independently selected from the group consisting of hydroxy and halo, (x) $-(C_0-C_6)$ alkyl-piperidinyl optionally substituted with one or more $-(C_1-C_6)$ alkyl which is optionally substituted with one or

more substituents independently selected from hydroxy and halo, (y) $-\text{SO}_2\text{-R}^{37}$, (z) $-\text{SO}_2\text{-NR}^{35}\text{R}^{36}$ or (a1) $-\text{S-phenyl-CH}_2\text{OH}$;

R^{38} is (a) $-(\text{C}_1\text{-C}_6)\text{alkyl}$, (b) $-(\text{C}_0\text{-C}_6)\text{alkyl-phenyl}$, (c) $-(\text{C}_0\text{-C}_6)\text{alkyl-phenanthrenyl}$ optionally substituted with one to three CF_3 , (d) $-(\text{C}_0\text{-C}_6)\text{alkyl-pyrrolidinyl}$ or (e) $-(\text{C}_0\text{-C}_6)\text{alkyl-morpholinyl}$;

or any two Z Groups for any occurrence in the same variable may be taken together to form (a) a carbocyclic ring of the formula $-(\text{CH}_2)_e-$ or (b) a heterocyclic ring selected from the group consisting of $-\text{O}(\text{CH}_2)_f\text{O}-$, $-(\text{CH}_2)_g\text{NH}-$ and $-\text{CH=CHNH}-$;

m is 0, 1 or 2;

n is 0, 1, 2 or 3;

b is 3, 4, 5, 6 or 7;

c, f, g, j and k are each independently 2, 3, 4, 5 or 6; and

e is 3, 4, 5, 6 or 7;

provided that in a compound of the above formula: 1) the substituent $\text{C}(\text{R}^{14})(\text{R}^{15})(\text{R}^{16})$ in R^4 is other than $(\text{C}_1\text{-C}_4)\text{alkyl}$; and 2) R^4 is halo only when R^8 is $-\text{C}(\text{O})\text{-OR}^9$ or $-\text{C}(\text{O})\text{NR}^{10}\text{R}^{11}$.

8. A method of claim 7 wherein the compound is selected from the group consisting of:

8-[[5-[2,6-dichloro-4-(4,5-dihydro-3,5-dioxo-1,2,4-triazine-2(3H)-yl)phenoxy]-2-hydroxyphenyl]sulfonyl]-spiro[8-azabicyclo[3.2.1]octane-3,2'-(3'H)-dihydro-furan];

2-{3,5-dichloro-4-[3-(3,3-dimethyl-piperidine-1-sulfonyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;

2-{3,5-dichloro-4-[4-hydroxy-3-(3-methyl-3-phenyl-piperidine-1-sulfonyl)-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;

N-cyclohexyl-5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-2-hydroxy-benzenesulfonamide;

N-bicyclo[2.2.1]hept-2-yl-5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-2-hydroxy-benzamide;

2-{3,5-dichloro-4-[3-(3,3-dimethyl-piperidine-1-carbonyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;

N-bicyclo[2.2.1]hept-2-yl-5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-2-hydroxy-benzamide;

2-{3,5-dichloro-4-[4-hydroxy-3-(3-methyl-3-phenyl-piperidine-1-carbonyl)-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;

5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-N-(6,6-dimethyl-bicyclo[3.1.1]hept-2-yl)-2-hydroxy-benzamide;

2-{3,5-dichloro-4-[3-(3,5-dimethyl-piperidine-1-carbonyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;

5 2-{3,5-dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;

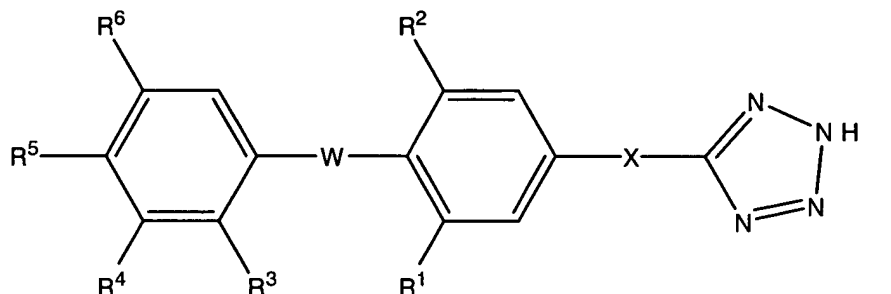
N-cyclohexyl-5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-2-hydroxy-benzamide;

10 2-{3,5-dichloro-4-[3-(3,4-dihydro-1H-isoquinoline-2-carbonyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;

2-{4-[3-(4-fluoro-benzyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-2H-[1,2,4]triazine-3,5-dione; and

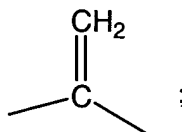
2-{3,5-dichloro-4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione.

15 9. A method for increasing the rate of nail growth in a mammal which comprises the administration to the mammal of an effective amount of a compound of the formula



or a stereoisomer, a pharmaceutically acceptable salt or prodrug thereof, or
20 a pharmaceutically acceptable salt of the prodrug, wherein:

W is O, S, SO, SO₂, CH₂, CF₂, CHF, C(=O), CH(OH), NR^a, or



X is O, CH₂, CH₂CH₂, S, SO, SO₂, CH₂NR^a, NR^a, or a bond;
25 each R^a is independently hydrogen, C₁-C₆alkyl, or C₁-C₆alkyl substituted with one substituent selected from C₃-C₆cycloalkyl or methoxy;

R^1 , R^2 , R^3 and R^6 are independently hydrogen, halogen, C_1 - C_8 alkyl, $-CF_3$, $-OCF_3$, $-OC_1$ - C_8 alkyl, or $-CN$;

R^4 is hydrogen, C_1 - C_{12} alkyl, [C_1 - C_{12} alkyl that is substituted with from one to three substituents independently selected from Group V], C_2 - C_{12} alkenyl,

- 5 C_2 - C_{12} alkynyl, halogen, $-CN$, $-OR^b$, $-SR^c$, $-S(=O)R^c$, $-S(=O)_2R^c$, aryl, heteroaryl, C_3 - C_{10} cycloalkyl, heterocycloalkyl, $-S(=O)_2NR^cR^d$, $-C(=O)NR^cR^d$, $-C(=O)OR^c$, $-NR^aC(=O)R^d$, $-NR^aC(=O)NR^cR^d$, $-NR^aS(=O)_2R^d$, $-NR^aR^d$, $-C(=O)R^c$,

- or R^3 and R^4 may be taken together with the carbon atoms to which they are attached to form an unsubstituted or substituted carbocyclic ring of formula $-(CH_2)_i-$
 10 or an unsubstituted or substituted heterocyclic ring selected from the group consisting of $-Q-(CH_2)_i-$ and $-(CH_2)_k-Q-(CH_2)_l-$ wherein Q is O, S or NR^a ; i is 3, 4, 5, 6 or 7; j is 2, 3, 4, 5, or 6; k and l are each independently 1, 2, 3, 4, or 5, and any substituents up to four are selected from C_1 - C_4 alkyl, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^aR^g$;

- 15 R^b is hydrogen, C_1 - C_{12} alkyl, [C_1 - C_{12} alkyl substituted with one to three substituents independently selected from Group V], aryl, heteroaryl, C_3 - C_{10} cycloalkyl, heterocycloalkyl, $-C(=O)NR^cR^d$, or $-C(=O)R^f$;

- R^c and R^d are each independently selected from hydrogen, C_1 - C_{12} alkyl, [C_1 - C_{12} alkyl substituted with one to three substituents independently selected from
 20 Group VI], C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, aryl, heteroaryl, C_3 - C_{10} cycloalkyl, heterocycloalkyl,

- or R^c and R^d may together along with the atom(s) to which they are attached form a 3-10 membered unsubstituted or substituted heterocyclic ring, which may contain a second heterogroup selected from O, NR^g , or S, wherein any
 25 substituents up to four are selected from C_1 - C_4 alkyl, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^aR^g$;

R^5 is $-OH$, $-OC_1$ - C_6 alkyl, $-OC(=O)R^f$, $-F$, $-C(=O)OR^c$,

- or R^4 and R^5 may together with the atom(s) to which they are attached form a heterocyclic ring selected from the group consisting of $-CR^c=CR^a-NH-$, $-N=CR^a-$
 30 $NH-$, $-CR^c=CR^a-O-$, $-CR^c=CR^a-S-$, $-CR^c=N-NH-$, or $-CR^a=CR^a-CR^a=N-$;

Group V is halogen, $-CF_3$, $-OCF_3$, hydroxy, oxo, C_1 - C_6 alkoxy, $-CN$, aryl, heteroaryl, C_3 - C_{10} cycloalkyl, heterocycloalkyl, $-SR^f$, $-S(=O)R^f$, $-S(=O)_2R^f$, [$-S(=O)_2NR^aR^f$, wherein R^a and R^f may together along with the atom(s) to which they are attached form a 3-8 membered heterocyclic ring, which may contain

a second heterogroup selected from O, NR^g or S], -NR^aR^g, or [-C(=O)NR^aR^f, wherein R^a and R^f may together along with the atom(s) to which they are attached form a 3-8 membered heterocyclic ring, which may contain a second heterogroup selected from O, NR^g or S];

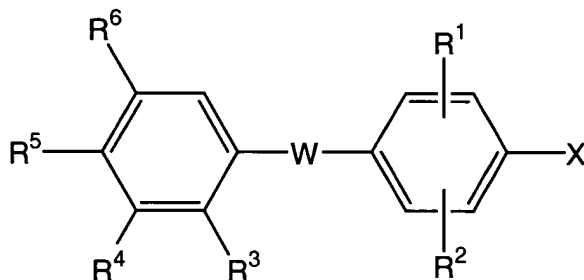
5 Group VI is halogen, hydroxy, oxo, C₁-C₆alkoxy, aryl, heteroaryl, C₃-C₈cycloalkyl, heterocycloalkyl, -CN, or -OCF₃;

R^g is hydrogen, -CN, C₁-C₁₀alkyl, [C₁-C₁₀alkyl substituted with one to three substituents independently selected from Group V], C₂-C₁₀alkenyl, C₂-C₁₀alkoxy, C₃-C₁₀cycloalkyl, aryl, heteroaryl, -C(=O)R^f, -C(=O)OR^f, -C(=O)NR^aR^f, -S(=O)₂NR^aR^f, or -S(=O)₂R^f;

R^f is hydrogen, C₁-C₁₀alkyl, [C₁-C₁₀alkyl substituted with from one to three substituents selected from Group VI], C₂-C₁₀alkenyl, C₂-C₁₀alkoxy, C₃-C₁₀cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; and

15 R^g is hydrogen, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆ alkenyl, aryl, -C(=O)R^f, -C(=O)OR^f, -C(=O)NR^aR^f, or -S(=O)₂R^f, provided that R¹ and R² are not both hydrogen, further provided that when X is CH₂, W is NR^a, R³ is hydrogen and R⁵ is -OH, then R⁶ and R⁴ are not both -C(CH₃)₃, further provided that when X is CH₂ or CH₂CH₂, W is O, and R³ and R⁶ are hydrogen, then R⁴ is not halogen, -CF₃, C₁-C₆alkyl or C₃-C₇cycloalkyl, and further provided that when R³ and R⁴ are hydrogen and W is O then R⁶ is not halogen, -CF₃, C₁-C₆alkyl or C₃-C₇cycloalkyl.

20 10. A method for increasing the rate of nail growth in a mammal which comprises the administration to the mammal of an effective amount of a compound of the formula



25

a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of said compound, stereoisomer, or prodrug, wherein:

W is oxygen, sulfur, -SO-, -S(O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NR^a, or -C(=CH₂)-

R^1 , R^2 , R^3 , and R^6 are each independently hydrogen, halogen, $-(C_1-C_8)$ alkyl, $-CF_3$, $-OCF_3$, $-O(C_1-C_8)$ alkyl, or $-CN$;

R^4 is hydrogen, $-(C_1-C_{12})$ alkyl substituted with zero to three substituents independently selected from Group V, $-(C_2-C_{12})$ alkenyl, $-(C_2-C_{12})$ alkynyl, halogen,
 5 CN , $-OR^b$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, aryl, heteroaryl, $-(C_3-C_{10})$ cycloalkyl, heterocycloalkyl, $-S(O)_2NR^cR^d$, $-C(O)NR^cR^d$, $-C(O)OR^c$, $-NR^aC(O)R^d$, $-NR^aC(O)NR^cR^d$, $-NR^aS(O)_2R^d$, or $-C(O)R^c$; or

R^3 and R^4 are taken together along with the carbon atoms to which they are attached to form a carbocyclic ring of formula $-(CH_2)_i-$ or a heterocyclic ring of
 10 formula $-(CH_2)_k-Q-(CH_2)_l-$ wherein Q is oxygen, sulfur, or $-NR^e-$; i is 3, 4, 5, or 6; k is 0, 1, 2, 3, 4, or 5; and l is 0, 1, 2, 3, 4, or 5; and wherein said carbocyclic ring and said heterocyclic ring are each substituted with zero to four substituents independently selected from $-(C_1-C_4)$ alkyl, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^aR^g$;

R^5 is hydroxy, $-O(C_1-C_6)$ alkyl, $-OC(O)R^f$, fluorine, or $-C(O)OR^c$; or

15 R^4 and R^5 are taken together along with the carbon atoms to which they are attached to form a heterocyclic ring selected from the group consisting of $-CR^c=CR^a-NH-$, $-N=CR^a-NH-$, $-CR^c=CR^a-O-$, $-CR^c=CR^a-S-$, $-CR^c=N-NH-$, and $-CR^a=CR^a-CR^a=N-$;

R^a for each occurrence is independently hydrogen, or $-(C_1-C_6)$ alkyl
 20 substituted with zero or one $-(C_3-C_6)$ cycloalkyl or methoxy;

R^b for each occurrence is independently hydrogen, $-(C_1-C_{12})$ alkyl substituted with zero to three substituents independently selected from Group V, aryl, heteroaryl, $-(C_3-C_{10})$ cycloalkyl, heterocycloalkyl, $-C(O)NR^cR^d$, or $-C(O)R^f$;

R^c and R^d for each occurrence are each independently hydrogen, $-(C_1-C_{12})$ alkyl substituted with zero to three substituents independently selected from
 25 Group VI, $-(C_2-C_{12})$ alkenyl, $-(C_2-C_{12})$ alkynyl, aryl, heteroaryl, $-(C_3-C_{10})$ cycloalkyl, or heterocycloalkyl;

provided that when R^4 is the moiety $-SR^c$, $-S(O)R^c$, or $-S(O)_2R^c$, R^c is other than hydrogen; or

30 R^c and R^d are taken together along with the atom(s) to which they are attached to form a 3-10 membered heterocyclic ring which may optionally contain a second heterogroup selected from oxygen, $-NR^e-$, or sulfur; and wherein said heterocyclic ring is substituted with zero to four substituents independently selected from $-(C_1-C_4)$ alkyl, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^aR^g$;

R^g for each occurrence is hydrogen, -CN, -(C₁-C₁₀)alkyl substituted with zero to three substituents independently selected from Group V, -(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkoxy, -(C₃-C₁₀)cycloalkyl, aryl, heteroaryl, -C(O)R^f, -C(O)OR^f, -C(O)NR^aR^f, or -S(O)₂R^f;

5 R^f for each occurrence is independently -(C₁-C₁₀)alkyl substituted with zero to three substituents independently selected from Group VI, -(C₂-C₁₂)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl, aryl, heteroaryl, or heterocycloalkyl;

R^g for each occurrence is independently hydrogen, -(C₁-C₆)alkyl, -(C₂-C₆)alkenyl, aryl, -C(O)R^f, -C(O)OR^f, -C(O)NR^aR^f, -S(O)₂R^f, or -(C₃-C₈)cycloalkyl;

10 Group V is halogen, -CF₃, -OCF₃, -OH, oxo, -(C₁-C₆)alkoxy, -CN, aryl, heteroaryl, -(C₃-C₁₀)cycloalkyl, heterocycloalkyl, -SR^f, -S(O)R^f, -S(O)₂R^f, -S(O)₂NR^aR^f, -NR^aR^g, or -C(O)NR^aR^f;

Group VI is halogen, hydroxy, oxo, -(C₁-C₆)alkoxy, aryl, heteroaryl, -(C₃-C₈)cycloalkyl, heterocycloalkyl, -CN, or -OCF₃;

15 provided that when R⁴ is -(C₁-C₁₂)alkyl substituted with zero to three substituents independently selected from Group V, wherein said Group V substituent is oxo, said oxo group is substituted on a carbon atom other than the C₁ carbon atom in -(C₁-C₁₂)alkyl;

20 aryl for each occurrence is independently phenyl or naphthyl substituted with zero to four substituents independently selected from halogen, -(C₁-C₆)alkyl, -CN, -SR^f, -S(O)R^f, -S(O)₂R^f, -(C₃-C₆)cycloalkyl, -S(O)₂NR^aR^f, -NR^aR^g, -C(O)NR^aR^f, -OR^b, -perfluoro-(C₁-C₄)alkyl, or -COOR^f;

25 provided that when said substituent(s) on aryl are -SR^f, -S(O)R^f, -S(O)₂R^f, -S(O)₂NR^aR^f, -NR^aR^g, -C(O)NR^aR^f, -OR^b, or -COOR^f, said substituents R^b, R^f, and R^g, are other than aryl or heteroaryl;

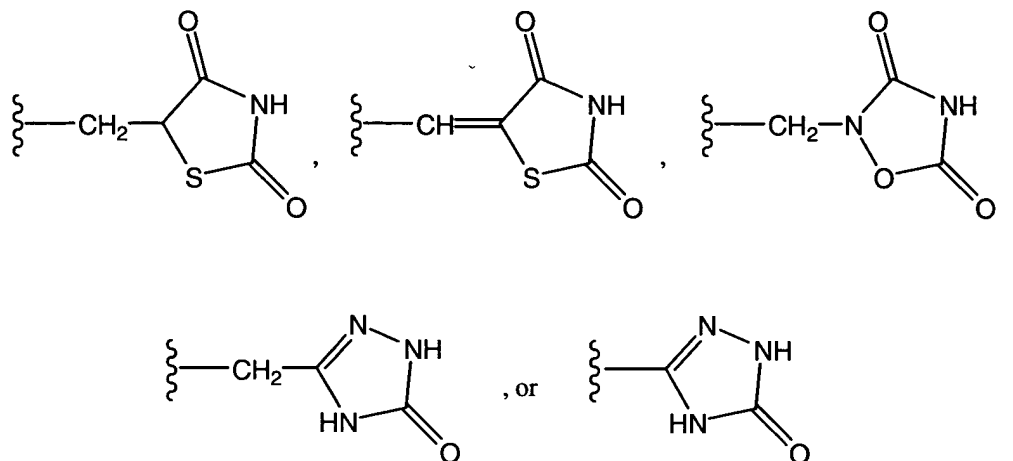
heteroaryl for each occurrence is independently a 5-, 6-, 7-, 8-, or 9-membered monocyclic or bicyclic ring having from one to three heteroatoms selected from O, N, or S;

30 wherein in said bicyclic ring, a monocyclic heteroaryl ring is fused to a benzene ring or to another heteroaryl ring, and having zero to three substituents independently selected from halogen, -(C₁-C₄)alkyl, -CF₃, -OR^b, -NR^aR^g, or -COOR^f;

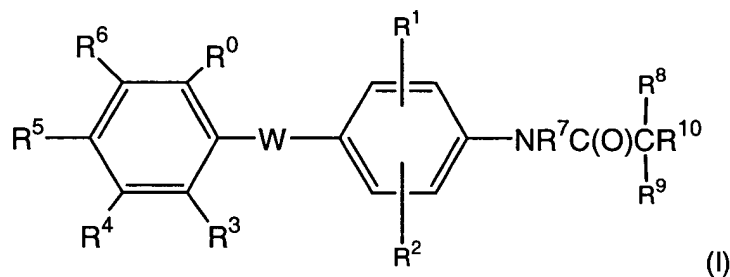
provided that when said substituent(s) on heteroaryl are -NR^aR^g, -OR^b, or -COOR^f, said substituents R^b, R^f, and R^g, are other than aryl or heteroaryl;

- heterocycloalkyl for each occurrence is independently a 5-, 6-, 7-, 8-, or 9-membered monocyclic or bicyclic cycloalkyl ring having from one to three heteroatoms selected from oxygen, $-NR^e$, or sulfur, and having zero to four substituents independently selected from $-(C_1-C_4)$ alkyl, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^aR^g$; and

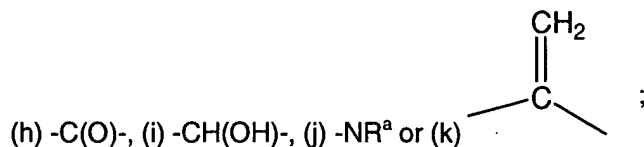
X is



11. A method for increasing the rate of nail growth in a mammal which comprises the administration to the mammal of an effective amount of a compound of the formula



- an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug; wherein W is (a) $-O-$, (b) $-S-$, (c) $-SO-$, (d) $-SO_2-$, (e) $-CH_2-$, (f) $-CF_2-$, (g) $-CHF-$,



R^0 is (a) hydrogen, (b) $-(C_1-C_6)$ alkyl substituted with zero or one substituent selected from the group consisting of (1) $-(C_3-C_6)$ cycloalkyl, (2) heterocycloalkyl and (3) phenyl substituted with zero or one substituent selected from the group consisting of (i) $-(C_1-C_4)$ alkyl, (ii) halogen, (iii) $-CF_3$ and (iv) $-OCF_3$; (c) $-C(O)R^h$, (d) $-S(O)_2R^h$ or
5 (e) halogen;

R^1 , R^2 , R^3 and R^6 are each independently (a) hydrogen, (b) halogen, (c) $-(C_1-C_8)$ alkyl, (d) $-CF_3$, (e) $-OCF_3$, (f) $-O(C_1-C_8)$ alkyl, or (g) $-CN$;

R^4 is (a) hydrogen, (b) $-(C_1-C_{12})$ alkyl substituted with zero to three substituents independently selected from Group V, (c) $-(C_2-C_{12})$ alkenyl, (d) $-(C_2-C_{12})$ alkynyl, (e)
10 halogen, (f) $-CN$, (g) $-OR^b$, (h) $-SR^c$, (i) $-S(O)R^c$, (j) $-S(O)_2R^c$, (k) aryl, (l) heteroaryl, (m) $-(C_3-C_{10})$ cycloalkyl, (n) heterocycloalkyl, (o) $-S(O)_2NR^cR^d$, (p) $-C(O)NR^cR^d$, (q) $-C(O)OR^c$, (r) $-NR^aC(O)R^d$, (s) $-NR^aC(O)NR^cR^d$, (t) $-NR^aS(O)_2R^d$, (u) $-NR^aR^d$ or (v) $-C(O)R^c$;

or R^3 and R^4 are taken together along with the carbon atoms to which they
15 are attached to form a carbocyclic ring of formula $-(CH_2)_i-$ or a heterocyclic ring of formula $-(CH_2)_k-Q-(CH_2)_i-$ wherein Q is $-O-$, $-S-$ or $-NR^e-$; i is 3, 4, 5 or 6; k is 0, 1, 2, 3, 4 or 5; and l is 0, 1, 2, 3, 4 or 5; and wherein the carbocyclic ring and the heterocyclic ring are each substituted with zero to four substituents independently selected from (a) $-(C_1-C_4)$ alkyl, (b) $-OR^b$, (c) oxo, (d) $-CN$, (e) phenyl or (f) $-NR^aR^g$;

20 R^5 is (a) $-OH$, (b) $-O(C_1-C_6)$ alkyl, (c) $-OC(O)R^f$, (d) F, or (e) $-C(O)OR^c$;

or R^4 and R^5 are taken together along with the carbon atoms to which they are attached to form a heterocyclic ring selected from the group consisting of $-CR^c=CR^a-NH-$, $-N=CR^a-NH-$, $-CR^c=CR^a-O-$, $-CR^c=CR^a-S-$, $-CR^c=N-NH-$ and $-CR^a=CR^a-CR^a=N-$;

25 R^7 is (a) hydrogen or (b) $-(C_1-C_6)$ alkyl;

R^8 and R^9 are each independently (a) hydrogen, (b) $-(C_1-C_6)$ alkyl, (c) aryl, or (d) halogen;

R^{10} is (a) $-(C_0-C_1)$ alkyl- $C(O)OH$, (b) $-(C_0-C_1)$ alkyl- $C(O)OR^f$, (c) $-(C_0-C_1)$ alkyl- $C(O)NR^cR^d$, or (d) $-(C_0-C_1)$ alkyl- OH ;

30 R^a for each occurrence is independently (a) hydrogen or (b) $-(C_1-C_6)$ alkyl substituted with zero or one $-(C_3-C_6)$ cycloalkyl or methoxy;

R^b for each occurrence is independently (a) hydrogen, (b) $-(C_1-C_{12})$ alkyl substituted with zero to three substituents independently selected from Group V, (c)

aryl, (d) heteroaryl, (e) $-(C_3-C_{10})$ cycloalkyl, (f) heterocycloalkyl, (g) $-C(O)NR^cR^d$, or (h) $-C(O)R^f$;

R^c and R^d for each occurrence are each independently (a) hydrogen, (b) $-(C_1-C_{12})$ alkyl substituted with zero to three substituents independently selected from
5 Group VI, (c) $-(C_2-C_{12})$ alkenyl, (d) $-(C_2-C_{12})$ alkynyl, (e) aryl, (f) heteroaryl, (g) $-(C_3-C_{10})$ cycloalkyl or (h) heterocycloalkyl;

provided that when R^d is the moiety $-SR^c$, $-S(O)R^c$ or $-S(O)_2R^c$, R^c is other than hydrogen;

or R^c and R^d are taken together along with the atom(s) to which they are
10 attached to form a 3-10 membered heterocyclic ring which may optionally contain a second heterogroup selected from $-O-$, $-NR^e$ or $-S-$; and wherein the heterocyclic ring is substituted with zero to four substituents independently selected from (a) $-(C_1-C_4)$ alkyl, (b) $-OR^b$, (c) oxo, (d) $-CN$, (e) phenyl or (f) $-NR^aR^g$;

R^e for each occurrence is (a) hydrogen, (b) $-CN$, (c) $-(C_1-C_{10})$ alkyl substituted
15 with zero to three substituents independently selected from Group V, (d) $-(C_2-C_{10})$ alkenyl, (e) $-(C_2-C_{10})$ alkoxy, (f) $-(C_3-C_{10})$ cycloalkyl, (g) aryl, (h) heteroaryl, (i) $-C(O)R^f$, (j) $-C(O)OR^f$, (k) $-C(O)NR^aR^f$ or (l) $-S(O)_2R^f$;

R^f for each occurrence is independently (a) $-(C_1-C_{10})$ alkyl substituted with zero
to three substituents independently selected from the Group VI, (b) $-(C_2-C_{10})$ alkenyl,
20 (c) $-(C_2-C_{10})$ alkynyl, (d) $-(C_3-C_{10})$ cycloalkyl, (e) aryl, (f) heteroaryl or (g) heterocycloalkyl;

R^g for each occurrence is independently (a) hydrogen, (b) $-(C_1-C_6)$ alkyl, (c) $-(C_2-C_6)$ alkenyl, (d) aryl, (e) $-C(O)R^f$, (f) $-C(O)OR^f$, (g) $-C(O)NR^aR^f$, (h) $-S(O)_2R^f$ or (i) $-(C_3-C_8)$ cycloalkyl;

R^h is (a) $-(C_1-C_6)$ alkyl substituted with zero or one substituent selected from
the group consisting of (1) $-(C_3-C_6)$ cycloalkyl, (2) heterocycloalkyl and (3) phenyl
substituted with zero or one substituent selected from the group consisting of (i) $-(C_1-C_4)$ alkyl, (ii) halogen, (iii) $-CF_3$ and (iv) $-OCF_3$; (b) phenyl substituted with zero to two
substituents independently selected from the group consisting of (1) $-(C_1-C_4)$ alkyl, (2)
25 halogen, (3) $-CF_3$ and (4) $-OCF_3$; (c) $-(C_3-C_6)$ cycloalkyl or (d) heterocycloalkyl;

Group V is (a) halogen, (b) $-CF_3$, (c) $-OCF_3$, (d) $-OH$, (e) $-oxo$, (f) $-(C_1-C_6)$ alkoxy, (g) $-CN$, (h) aryl, (i) heteroaryl, (j) $-(C_3-C_{10})$ cycloalkyl, (k) heterocycloalkyl,
30 (l) $-SR^f$, (m) $-S(O)R^f$, (n) $-S(O)_2R^f$, (o) $-S(O)_2NR^aR^f$ (p) $-NR^aR^g$ or (q) $-C(O)NR^aR^f$;

Group VI is (a) halogen, (b) hydroxy, (c) oxo, (d) $-(C_1-C_6)alkoxy$, (e) aryl, (f) heteroaryl, (g) $-(C_3-C_8)cycloalkyl$, (h) heterocycloalkyl, (i) $-CN$, or (j) $-OCF_3$;

provided that when the substituent R^4 is $-(C_1-C_{12})alkyl$ substituted with zero to three substituents independently selected from Group V wherein the Group V
5 substituent is oxo, the oxo group is substituted on a carbon atom other than the C_1 carbon atom in $-(C_1-C_{12})alkyl$;

aryl for each occurrence is independently phenyl or naphthyl substituted with zero to four substituents independently selected from (a) halogen, (b) $-(C_1-C_6)alkyl$, (c) $-CN$, (d) $-SR^f$, (e) $-S(O)R^f$, (f) $-S(O)_2R^f$, (g) $-(C_3-C_6)cycloalkyl$, (h) $-S(O)_2NR^aR^f$, (i) $-NR^aR^g$, (j) $-C(O)NR^aR^f$, (k) $-OR^b$, (l) $-perfluoro-(C_1-C_4)alkyl$, or (m) $-COOR^f$;

10 provided that when the substituent(s) on aryl are $-SR^f$, $-S(O)R^f$, $-S(O)_2R^f$, $-S(O)_2NR^aR^f$, $-NR^aR^g$, $-C(O)NR^aR^f$, $-OR^b$, or $-COOR^f$, the substituents R^b , R^f and R^g are other than aryl or heteroaryl;

heteroaryl for each occurrence is independently a 5-, 6-, 7-, 8-, 9- or 10-
15 membered monocyclic or bicyclic ring having from 1 to 3 heteroatoms selected from O, N or S; wherein in the bicyclic ring, a monocyclic heteroaryl ring is fused to a benzene ring or to another heteroaryl ring; and having zero to three substituents independently selected from (a) halogen, (b) $-(C_1-C_4)alkyl$, (c) $-CF_3$, (d) $-OR^b$, (e) $-NR^aR^g$, or (f) $-CO_2R^f$;

20 provided that when the substituent(s) on heteroaryl are $-OR^b$, $-NR^aR^g$ or $-CO_2R^f$, the substituents R^b , R^f and R^g are other than aryl or heteroaryl;

heterocycloalkyl for each occurrence is independently a 4-, 5-, 6-, 7-, 8-, 9- or 10-membered monocyclic or bicyclic cycloalkyl ring having from 1 to 3 heteroatoms selected from O, NR^g or S; and having zero to four substituents independently
25 selected from (a) $-(C_1-C_4)alkyl$, (b) $-OR^b$, (c) oxo, (d) $-CN$, (e) phenyl or (f) $-NR^aR^g$.

12. A method of claim 11 which comprises administering a compound selected from the group consisting of:

N-{4-[3-(cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-malonamic acid;

30 N-{3-chloro-4-[4-hydroxy-3-(1-isopropyl-2-methyl-propylcarbamoyl)-phenoxy]-5-methyl-phenyl}-malonamic acid;

N-{3,5-dichloro-4-[3-((1S)-cyclohexyl-ethylcarbamoyl)-4-hydroxy-phenoxy]-phenyl}-malonamic acid;

- N-[3,5-dichloro-4-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-malonamic acid;
- N-[3,5-dichloro-4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-malonamic acid;
- 5 N-[3-chloro-4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- N-[4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- 10 N-[4-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- N-[3-chloro-4-(3-cyclopropylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- 15 N-[3,5-dichloro-4-(3-cyclopropylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-malonamic acid;
- N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[3,5-dichloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-malonamic acid;
- 20 N-[4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-2-methyl-malonamic acid;
- 25 N-[3-chloro-4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-2-methyl-malonamic acid;
- N-[3-chloro-4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- 30 N-[4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl]-malonamic acid;

- N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-malonamic acid;
- N-{4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-malonamic acid;
- 5 N-[4-(3-cyclopentylacetyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-(4-{3-[(4-fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-3,5-dimethyl-phenyl)-malonamic acid;
- 10 N-{4-[3-(2-cyclopentyl-1-hydroxy-ethyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-malonamic acid;
- N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid methyl ester;
- N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid ethyl ester;
- 15 N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid ethyl ester;
- N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid methyl ester;
- 20 N-[3-chloro-4-(3-cyclopentanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- N-[4-(3-cyclopentanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-malonamic acid;
- 25 N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-malonamic acid methyl ester;
- N-{3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl}-malonamic acid methyl ester;
- N-{3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl}-malonamic acid ethyl ester;
- 30 N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-2-methyl-malonamic acid methyl ester;
- N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-2-methyl-malonamic acid;

N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-2-methyl-malonamic acid methyl ester;

N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-2-methyl-malonamic acid;

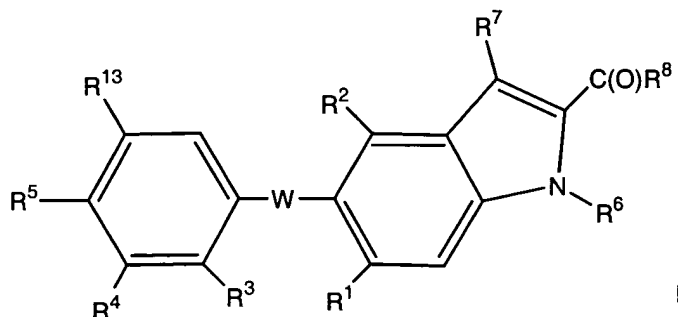
5 N-{3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl}-2-methyl-malonamic acid methyl ester; and

N-{3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl}-2-methyl-malonamic acid;

10 N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-malonamic acid; and

N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-malonamic acid methyl ester; or an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug.

15 13. A method for increasing the rate of nail growth in a mammal which comprises the administration to the mammal of an effective amount of a compound of the formula



20 or the pharmaceutically acceptable salt thereof; wherein

W is oxygen, CH₂, CF₂, NR¹², S(O)_m wherein m is 0, 1 or 2;

R¹, R², and R³ are each independently selected from the group consisting of hydrogen, halo, cyano, trifluoromethyl, trifluomethoxy and (C₁-C₆)alkyl;

25 R⁴ is hydrogen, halo, cyano, (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, (C₃-C₁₀)cycloalkyl, (C₃-C₁₀)cycloalkyl(C₁-C₆)alkyl, (C₆-C₁₀)aryl, (C₆-C₁₀)aryl(C₁-C₆)alkyl, (C₂-C₉)heteroaryl, (C₂-C₉)heteroaryl(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkyl, -OR⁹, -S(O)₂NR¹⁰R¹¹, -C(O)NR¹⁰R¹¹, -C(O)R¹⁰, -

CH(OH)R^{10} , $-\text{NR}^{12}\text{C(O)R}^{10}$, $-\text{NR}^{12}\text{C(O)NR}^{10}\text{R}^{11}$, $-\text{NR}^{12}\text{S(O)}_2\text{R}^{10}$ or $-\text{S(O)}_n\text{R}^{10}$

wherein n is 0, 1 or 2;

R^5 is hydroxy, fluoro, $(\text{C}_1\text{-C}_4)\text{alkoxy}$ or $-\text{OC(O)R}^{10}$;

R^6 is hydrogen, $-\text{C(O)CH}_3$ or $(\text{C}_1\text{-C}_6)\text{alkyl}$;

5 R^7 is hydrogen or $(\text{C}_1\text{-C}_6)\text{alkyl}$;

R^8 is OR^{12} or NR^9R^{12} ;

R^9 for each occurrence is independently hydrogen, $(\text{C}_1\text{-C}_{12})\text{alkyl}$, $(\text{C}_3\text{-C}_{10})\text{cycloalkyl}$, $(\text{C}_2\text{-C}_9)\text{heterocycloalkyl}$, $(\text{C}_6\text{-C}_{10})\text{aryl}$ or $(\text{C}_2\text{-C}_9)\text{heteroaryl}$;

10 R^{10} for each occurrence is independently hydrogen, $(\text{C}_1\text{-C}_{12})\text{alkyl}$, $(\text{C}_2\text{-C}_{12})\text{alkenyl}$, $(\text{C}_2\text{-C}_{12})\text{alkynyl}$, $(\text{C}_3\text{-C}_{10})\text{cycloalkyl}$, $(\text{C}_3\text{-C}_9)\text{cycloalkyl}(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_6\text{-C}_{10})\text{aryl}$, $(\text{C}_2\text{-C}_9)\text{heteroaryl}$ or $\text{halo}(\text{C}_6\text{-C}_{10})\text{aryl}$;

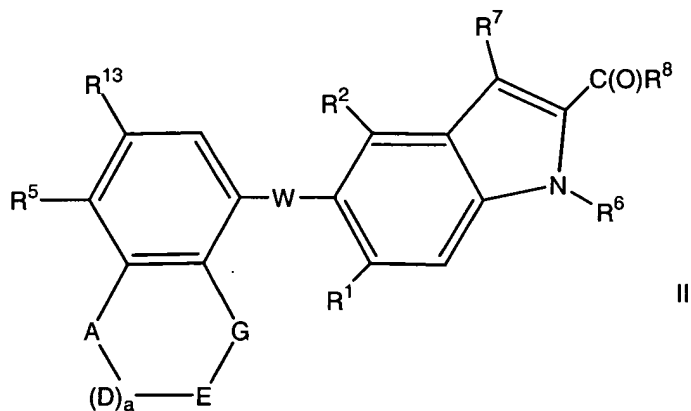
R^{11} for each occurrence is independently hydrogen, $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_3\text{-C}_{10})\text{cycloalkyl}$ or $(\text{C}_3\text{-C}_9)\text{cycloalkyl}(\text{C}_1\text{-C}_6)\text{alkyl}$;

15 or R^{10} and R^{11} may be taken together with the nitrogen to which they are attached to form a 3 to 10 membered heterocyclic group which may contain a second heteroatom selected from oxygen, sulfur or NR^{14} wherein R^{14} is hydrogen or $(\text{C}_1\text{-C}_6)\text{alkyl}$;

R^{12} for each occurrence is independently hydrogen or $(\text{C}_1\text{-C}_6)\text{alkyl}$;

R^{13} is hydrogen, halo or $(\text{C}_1\text{-C}_6)\text{alkyl}$;

20 or R^3 and R^4 may be taken together with the carbons to which they are attached to form a compound of the formula



wherein a is 0, 1, 2 or 3;

25 A, D, E and G are each independently selected from the group consisting of $\text{CR}^{16}\text{R}^{17}$, NR^{18} , oxygen or sulfur;

R¹⁶ and R¹⁷ for each occurrence are each independently selected from hydrogen or (C₁-C₆)alkyl; and

R¹⁸ is hydrogen, (C₁-C₆)alkyl, -C(O)R¹⁰ or -S(O)₂R¹⁰ wherein R¹⁰ is defined as above.

- 5 14. A method of claim 13 wherein the compound is selected from the group consisting of:
- 5-(4-Hydroxy-3-isopropyl-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
 4,6-Dichloro-5-(4-hydroxy-3-isopropyl-phenoxy)-1H-indole-2-carboxylic acid;
 5-(3-sec-butyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
10 5-[3-(4-Fluoro-benzyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
 5-{3-[(4-Fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-4,6-dimethyl-1H-indole-2-carboxylic acid;
 5-[3-(2-Cyclopentyl-1-hydroxy-ethyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
15 5-[3-(4-Fluoro-benzoyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
 5-[3-(Cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
20 5-(3-Cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
 4,6-Dichloro-5-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-1H-indole-2-carboxylic acid;
 4,6-Dichloro-5-(4-hydroxy-3-isopropyl-phenoxy)-1-methyl-1H-indole-2-carboxylic acid;
25 4,6-Dichloro-5-(4-hydroxy-3-isopropyl-phenoxy)-3-methyl-1H-indole-2-carboxylic acid;
 5-[3-(4-Fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
30 5-[3-(4-Fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,4,6-trimethyl-1H-indole-2-carboxylic acid;
 4,6-Dichloro-5-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-1H-indole-2-carboxylic acid;

- 4-Chloro-50(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-5-methyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-[4-hydroxy-3-(1-isopropyl-2-methyl-propylcarbamoyl)-phenoxy]-1H-indole-2-carboxylic acid;
- 5 5-[3-(4-Fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-1,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 5{3-[(4-Fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-3,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 10 5-[3-(4-Fluoro-benzyl)-4-hydroxy-phenoxy]-3,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 5-(3-Cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-1H-indole-2-carboxylic acid;
- 15 5-(3-Cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 5-(3-Cyclopropylsulfamoyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 20 5-(4-Hydroxy-3-isopropyl-phenoxy)-3,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 5-(4-Hydroxy-3-isopropyl-phenoxy)-1,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-1H-indole-2-carboxylic acid;
- 25 4,6-Dichloro-5-[3-(4-fluoro-benzenesulfonyl-4-hydroxy-phenoxy)-3-methyl-1H-indole-2-carboxylic acid;
- 5-(3-Cyclobutylsulfamoyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 30 5-[4-Hydroxy-3-(1-isopropyl-2-methyl-propylcarbamoyl)-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-{3-[(4-fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-1H-indole-2-carboxylic acid;
- 5-(4-Hydroxy-2,3-dimethyl-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-(4-hydroxy-2,3-dimethyl-phenoxy)-1H-indole-2-carboxylic acid;

5-(7-Hydroxy-indan-4-yloxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
 4,6-Dichloro-5-(7-hydroxy-indan-4-yloxy)-1H-indole-2-carboxylic acid;
 4,6-Dichloro-5-(4-hydroxy-5,6,7,8-tetrahydro-naphthalen-1-yloxy)-1H-indole-2-carboxylic acid; and

5 5-(4-Hydroxy-5,6,7,8-tetrahydro-naphthalen-1-yloxy)-4,6-dimethyl-1H-indole-2-carboxylic acid.

15. A method of claim 1, 4, 6, 7, 9, 10, 11 or 13 wherein the compound is cardiac-sparing.

16. A method of claim 1, 4, 6, 7, 9, 10, 11 or 13 wherein the mammal is a human being.

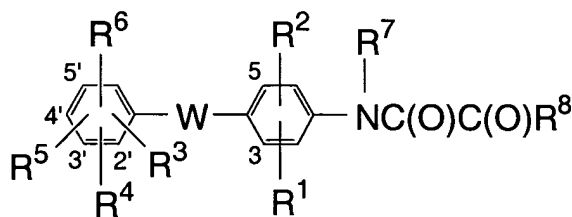
17. A method of claim 1, 4, 6, 7, 9, 10, 11 or 13 wherein the administration is topical.

18. A method of claim 1, 4, 6, 7, 9, 10, 11 or 13 wherein the effective amount of the compound is about 0.0001% to about 10% (w/v) of the compound per day.

19. A method of claim 1, 4, 6, 7, 9, 10, 11 or 13 which comprises the administration of an effective amount of a nail growth promoter, an antibacterial agent or an antifungal agent.

20. A method of claim 1, 4, 6, 7, 9, 10, 11 or 13 wherein the antifungal agent is fluconazole, itraconazole, terbinafine or ciclopirox.

21. A topical pharmaceutical composition for increasing the rate of nail growth which comprises an effective amount of a compound of the formula



25 a prodrug thereof, a geometric or optical isomer thereof, or a pharmaceutically acceptable salt of said compound, said prodrug, or said isomer, wherein:

R¹, R² and R³ are each independently hydrogen, halogen, C₁₋₆ alkyl, trifluoromethyl, -CN, -OCF₃ or -OC₁₋₆ alkyl;

R^4 is hydrogen, C_{1-12} alkyl optionally substituted with one to three substituents independently selected from Group Z, C_{2-12} alkenyl, halogen, -CN, aryl, heteroaryl, C_{3-10} cycloalkyl, heterocycloalkyl, $-S(O)_2NR^9R^{10}$, $-C(O)NR^9R^{10}$, $-(C_{1-6} \text{ alkyl})-NR^9R^{10}$, $-NR^9C(O)R^{10}$, $-NR^9C(O)NR^9R^{10}$, $-NR^9S(O)_2R^{10}$, $-(C_{1-6} \text{ alkyl})-OR^{11}$, -
5 OR^{11} or $-S(O)_aR^{12}$, provided that, where R^5 is not fluoro, R^4 is $-S(O)_2NR^9R^{10}$, $-C(O)NR^9R^{10}$, $-(C_{1-6} \text{ alkyl})-NR^9R^{10}$, $-NR^9C(O)R^{10}$, $-NR^9C(O)NR^9R^{10}$, $-NR^9S(O)_2R^{10}$, $-(C_{1-6} \text{ alkyl})-OR^{11}$, $-OR^{11}$ or $-S(O)_aR^{12}$;

or R^3 and R^4 may be taken together to form a carbocyclic ring A of the formula $-(CH_2)_b-$ or a heterocyclic ring A selected from the group consisting of $-Q-$
10 $(CH_2)_c-$ and $-(CH_2)_j-Q-(CH_2)_k-$ wherein Q is O, S or NR^{17} , wherein said carbocyclic ring A and said heterocyclic ring A are each independently optionally substituted with one or more substituents independently selected from C_{1-4} alkyl, halide or oxo;

R^5 is fluoro, hydroxy, C_{1-4} alkoxy or $OC(O)R^9$;

or R^4 and R^5 may be taken together to form a heterocyclic ring B selected
15 from the group consisting of $-CR^9=CR^{10}-NH-$, $-N=CR^9-NH-$, $-CR^9=CH-O-$ and $-CR^9=CH-S-$;

R^6 is hydrogen, halogen, C_{1-4} alkyl or trifluoromethyl;

R^7 is hydrogen or C_{1-6} alkyl;

R^8 is $-OR^9$ or $-NR^{19}R^{20}$;

R^9 and R^{10} for each occurrence are independently (A) hydrogen, (B) C_{1-12}
20 alkyl optionally substituted with one or more substituents independently selected from Group V, (C) C_{2-12} alkenyl, (D) C_{3-10} cycloalkyl optionally substituted with one or more substituents independently selected from C_{1-6} alkyl, C_{2-5} alkynyl, C_{3-10} cycloalkyl, -CN, $-NR^{13}R^{14}$, oxo, $-OR^{18}$, $-COOR^{18}$ or aryl optionally substituted with X and Y, (E) aryl optionally substituted with X and Y, or (F) het optionally substituted with X and Y;

or R^9 and R^{10} for any occurrence may be taken together to form a heterocyclic ring C optionally further containing a second heterogroup selected from the group consisting of $-O-$, $-NR^{13}-$ and $-S-$, and optionally further substituted with
30 one or more substituents independently selected from C_{1-5} alkyl, oxo, $-NR^{13}R^{14}$, $-OR^{18}$, $-C(O)_2R^{18}$, -CN, $-C(O)R^9$, aryl optionally substituted with X and Y, het optionally substituted with X and Y, C_{5-6} spirocycloalkyl, and a carbocyclic ring B selected from the group consisting of 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated carbocyclic rings, and including any bicyclic group in

which said carbocyclic ring B is fused to a carbocyclic ring C selected from the group consisting of 5-, 6-, 7-and 8-membered partially and fully saturated, and unsaturated carbocyclic rings;

5 R^{11} is C_{1-12} alkyl optionally substituted with one or more substituents independently selected from Group V, C_{2-12} alkenyl, C_{3-10} cycloalkyl, trifluoromethyl, difluoromethyl, monofluoromethyl, aryl optionally substituted with X and Y, het optionally substituted with X and Y, $-C(O)NR^9R^{10}$ or $-C(O)R^9$;

10 R^{12} is C_{1-12} alkyl optionally substituted with one or more substituents independently selected from Group V, C_{2-12} alkenyl, C_{3-10} cycloalkyl, aryl optionally substituted with X and Y, or het optionally substituted with X and Y;

15 R^{13} and R^{14} for each occurrence are independently hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, $-(C_{1-6} \text{ alkyl})-C_{1-6}$ alkoxy, aryl optionally substituted with X and Y, het optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -aryl optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -heterocycle optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -hydroxy, $-(C_{1-4} \text{ alkyl})$ -halo, $-(C_{1-4} \text{ alkyl})$ -poly-halo, $-(C_{1-4} \text{ alkyl})-CONR^{15}R^{16}$ or C_{3-10} cycloalkyl;

R^{15} and R^{16} for each occurrence are independently hydrogen, C_{1-6} alkyl, C_{3-10} cycloalkyl or aryl optionally substituted with X and Y;

R^{17} is hydrogen, C_{1-6} alkyl, $-COR^9$ or $-SO_2R^9$;

20 R^{18} is hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, $-(C_{1-6} \text{ alkyl})-C_{1-6}$ alkoxy, aryl optionally substituted with X and Y, het optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -aryl optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -heterocycle optionally substituted with X and Y, $-(C_{1-4} \text{ alkyl})$ -hydroxy, $-(C_{1-4} \text{ alkyl})$ -halo, $-(C_{1-4} \text{ alkyl})$ -poly-halo, $-(C_{1-4} \text{ alkyl})-CONR^{15}R^{16}$, $-(C_{1-4} \text{ alkyl})-(C_{1-4} \text{ alkoxy})$ or C_{3-10} cycloalkyl;

25 R^{19} is hydrogen or C_{1-6} alkyl;

R^{20} is hydrogen or C_{1-6} alkyl;

W is O, $S(O)_d$, CH_2 or NR^9 ;

30 Group Z is C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, $-CF_3$, $-OCF_3$, hydroxy, oxo, -CN, aryl, heteroaryl, C_{3-10} cycloalkyl, heterocycloalkyl, $-S(O)_aR^{12}$, $-S(O)_2NR^9R^{10}$, $-C(O)R^9R^{10}$, and $-NR^9R^{10}$;

Group V is halogen, $-NR^{13}R^{14}$, $-OCF_3$, $-OR^9$, oxo, trifluoromethyl, -CN, C_{3-10} cycloalkyl, aryl optionally substituted with X and Y, and het optionally substituted with X and Y;

het for each occurrence is a heterocyclic ring D selected from the group consisting of 4-, 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated, heterocyclic rings containing from one to four heteroatoms independently selected from the group consisting of N, O and S, and including any
5 bicyclic group in which said heterocyclic ring D is fused to a benzene ring or a heterocyclic ring E selected from the group consisting of 4-, 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated, heterocyclic rings containing from one to four heteroatoms independently selected from the group consisting of N, O and S;

10 X and Y for each occurrence are independently (A) hydrogen, (B) halogen, (C) trifluoromethyl, (D) $-OCF_3$, (E) $-CN$, (F) C_{1-6} alkyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, $-OCF_3$, $-CF_3$ and phenyl, (G) C_{1-6} alkoxy, (H) aryl optionally substituted with one or more substituents independently selected from the group consisting of halogen,
15 $-OCF_3$, $-CF_3$, C_{1-4} alkyl and C_{1-4} alkoxy, (I) $-C(O)_2R^{13}$, (J) $-C(O)NR^{13}R^{14}$, (K) $-C(O)R^{13}$, (L) $-NR^{13}C(O)NR^{13}R^{14}$ and (M) $-NR^{13}C(O)R^{14}$;

or X and Y for any occurrence in the same variable may be taken together to form (a) a carbocyclic ring D of the formula $-(CH_2)_e-$ or (b) a heterocyclic ring F selected from the group consisting of $-O(CH_2)_fO-$, $(CH_2)_gNH-$ and $-CH=CHNH-$;

20 a and d are each independently 0, 1 or 2;
b is 3, 4, 5, 6 or 7;
c, f, g, j and k are each independently 2, 3, 4, 5 or 6; and
e is 3, 4, 5, 6 or 7;
and a pharmaceutically acceptable carrier.

25 22. A composition of claim 21 wherein the compound is selected from the group consisting of:

N-[3-chloro-4-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-oxamic acid;

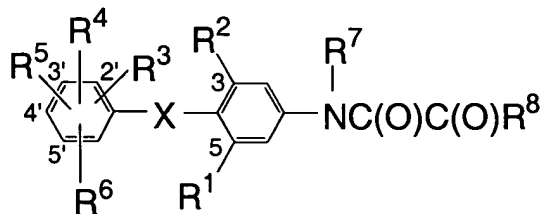
30 N-[4-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;

N-[4-[3-(cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl]-oxamic acid;

N-[3-chloro-4-[3-(cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-5-methyl-phenyl]-oxamic acid;

- N-[4-(7-hydroxy-indan-4-yloxy)-3,5-dimethyl-phenyl]-oxamic acid;
N-{3,5-dichloro-4-[3-(cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-phenyl}-oxamic acid;
N-[3,5-dichloro-4-(3-cyclopentanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;
5 N-[3,5-dichloro-4-(3-cyclopropylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;
N-[3,5-dichloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;
10 N-[4-(3-cyclopropylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;
N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-oxamic acid;
N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;
15 N-[4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;
N-[3-chloro-4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-oxamic acid;
20 N-[3,5-dichloro-4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;
N-[4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-oxamic acid;
N-[3-chloro-4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-oxamic acid;
25 N-[3,5-dichloro-4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-oxamic acid;
N-[3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl]-oxamic acid;
30 N-[4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl]-oxamic acid; and
N-[3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl]-oxamic acid.

23. A topical pharmaceutical composition for increasing the rate of nail growth which comprises an effective amount of a compound of the formula



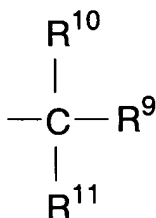
5 a prodrug thereof, a geometric or optical isomer thereof, or a pharmaceutically acceptable salt of said compound, said prodrug, or said isomer, wherein:

R¹ and R² are independently halogen, C₁₋₈ alkyl, -CN or C₁₋₈ perfluoroalkyl; provided that at least one of R¹ and R² is -CN;

10 R³ is hydrogen or C₁₋₈ alkyl;

R⁴ is halogen, C₁₋₈ perfluoroalkyl, C₁₋₈ alkyl, C₁₋₈ alkanoyl, hydroxy-(C₁₋₈ alkyl), aryl optionally substituted with Y and Z, aryl-(C₁₋₈ alkyl), carbocyclic aroyl optionally substituted with Y and Z, C₃₋₁₀ cycloalkyl optionally substituted with Y and Z, or C₃₋₁₀ cycloalkyl-(C₁₋₈ alkyl);

15 or R⁴ is the radical



wherein: R⁹ is hydrogen, C₁₋₈ alkyl, aryl optionally substituted with Y and Z, aryl-(C₁₋₈ alkyl), C₃₋₁₀ cycloalkyl optionally substituted with Y and Z, or C₃₋₁₀ cycloalkyl-(C₁₋₈ alkyl); R¹⁰ is -OR¹⁴; R¹¹ is hydrogen or C₁₋₈ alkyl; or R¹⁰ and R¹¹ may be taken

20 together with the carbon atom to which they are attached to form a carbonyl group;

R⁵ is hydroxy, esterified hydroxy or etherified hydroxy;

R⁶ is hydrogen, halogen, C₁₋₈ alkyl or C₁₋₈ perfluoroalkyl;

R⁷ is hydrogen, C₁₋₈ alkyl or C₁₋₈ perfluoroalkyl;

R⁸ is -OR¹² or -NR¹²R¹³;

25 R¹² and R¹³ are each independently hydrogen or C₁₋₈ alkyl;

R¹⁴ is hydrogen, C₁₋₈ alkyl or C₁₋₈ acyl;

X is O, S(O)_a, C=O or NR¹⁵;

a is 0, 1 or 2;

R¹⁵ is hydrogen or C₁₋₈ alkyl;

Y and Z for each occurrence are independently (a) hydrogen, (b) halogen, (c) trifluoromethyl, (d) -OCF₃, (e) -CN, (f) C₁₋₆ alkyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, -OCF₃, -CF₃ and phenyl, (g) C₁₋₆ alkoxy, (h) aryl optionally substituted with one or more substituents independently selected from the group consisting of halogen, -OCF₃, -CF₃, C₁₋₄ alkyl and C₁₋₄ alkoxy, (i) -C(O)₂R¹⁶, (j) -C(O)NR¹⁶R¹⁷, (k) -C(O)R¹⁶, (l) -NR¹⁶C(O)NR¹⁶R¹⁷ or (m) -NR¹⁶C(O)R¹⁷; or Y and Z for any occurrence may be taken together to form (a) a carbocycle of the formula -(CH₂)_b, or (b) a heterocycle selected from the group consisting of -O(CH₂)_cO-, -(CH₂)_dNH- and -CH=CHNH-;

b is 3, 4, 5, 6 or 7;

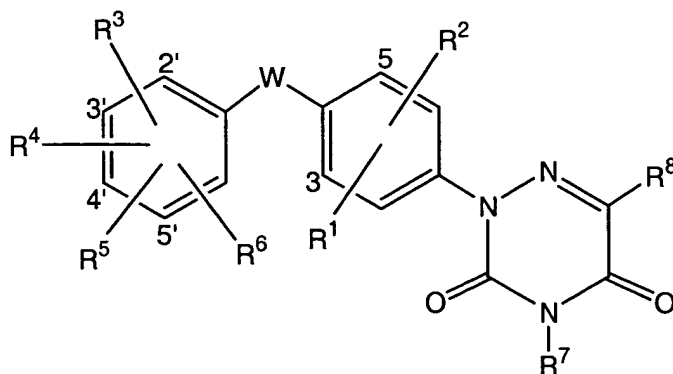
c and d are each independently 2, 3, 4, 5 or 6;

R¹⁶ and R¹⁷ for each occurrence are independently hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, -(C₁₋₆ alkyl)-C₁₋₆ alkoxy, aryl optionally substituted with X and Y, het optionally substituted with X and Y, -(C₁₋₄ alkyl)-aryl optionally substituted with X and Y, -(C₁₋₄ alkyl)-heterocycle optionally substituted with X and Y, -(C₁₋₄ alkyl)-hydroxy, -(C₁₋₄ alkyl)-halo, -(C₁₋₄ alkyl)-poly-halo, -(C₁₋₄ alkyl)-CONR¹⁸R¹⁹ or C₃₋₁₀ cycloalkyl;

het for each occurrence is a heterocyclic ring selected from the group consisting of 4-, 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated, heterocyclic rings containing from one to four heteroatoms independently selected from the group consisting of N, O and S, and including any bicyclic group in which said heterocyclic ring is fused to a benzene ring or a heterocyclic ring selected from the group consisting of 4-, 5-, 6-, 7- and 8-membered partially and fully saturated, and unsaturated, heterocyclic rings containing from one to four heteroatoms independently selected from the group consisting of N, O and S; and

R¹⁸ and R¹⁹ for each occurrence are independently hydrogen, C₁₋₆ alkyl, C₃₋₁₀ cycloalkyl or aryl optionally substituted with Y and Z; and a pharmaceutically acceptable carrier.

24. A topical pharmaceutical composition for increasing the rate of nail growth which comprises an effective amount of a compound of the formula



- an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug; wherein W is (a) -O-, (b) -S(O)_m-, (c) -NR³⁰-, (d) -C(O)-, (e) -HC=CH-, (f) -CH₂-, (g) -CHF-, (h) -CF₂- or (i) -CH(OH)-;
- 5 R¹ and R² are independently (a) hydrogen, (b) halogen, (c) -(C₁-C₆)alkyl, (d) -CN, (e) -OR¹² or (f) -trifluoromethyl;
- R³ is (a) hydrogen, (b) halogen, (c) -(C₁-C₆)alkyl optionally substituted with one to three substituents independently selected from the group consisting of
- 10 halogen, -OCF₃ and -CF₃, (d) -CN, (e) -OR¹², (f) -trifluoromethyl, (g) -NO₂, (h) -SO₂-R¹³, (i) -C(O)₂R⁹, (j) -C(O)NR¹⁹R²⁰, (k) -C(O)R¹⁶, (l) -NR²¹C(O)-NR²¹R²², (m) -NR¹⁹-C(O)R²⁰ or (n) -NR¹⁷R¹⁸;
- R⁴ is (a) -C(R¹⁴)(R¹⁵)(R¹⁶), (b) -(C₀-C₃)alkyl-NR¹⁷R¹⁸, (c) -C(O)NR¹⁹R²⁰, (d) -NR¹⁹-C(O)-R²⁰, (e) -(C₀-C₃)alkyl-NR²¹-C(O)-NR²¹R²², (f) -S(O)_m-R²², (g) -S(O)₂-NR²¹R²², (h) -NR²¹-S(O)₂-R²², (i) -aryl, (j) -het, (k) -OR³³ or (l) halogen; provided that
- 15 in substituents (f) and (h), R²² is other than -OR³⁴; and provided that when substituent (b) is -(C₀)alkyl-NR¹⁷R¹⁸, R¹⁸ is other than -C(O)-R²⁸ or -S(O)₂-R²⁹;
- or R³ and R⁴ may be taken together to form a carbocyclic ring of Formula - (CH₂)_b- or a heterocyclic ring selected from the group consisting of -Q-(CH₂)_c- and - (CH₂)_j-Q-(CH₂)_k- wherein Q is O, S or NR²⁵; wherein said carbocyclic ring is optionally substituted with one or more substituents independently selected from Group V; and wherein said heterocyclic ring is optionally substituted with one or more substituents independently selected from Group Z;
- 20 R⁵ is -OR²³;
- or R⁴ and R⁵ may be taken together to form a heterocyclic ring selected from the group consisting of -CR³¹=CR³²-NH-, -N=CR³¹-NH-, -CR³¹=CR³²-O- and - CR³¹=CR³²-S-;
- 25 or R⁴ and R⁵ may be taken together to form a heterocyclic ring selected from the group consisting of -CR³¹=CR³²-NH-, -N=CR³¹-NH-, -CR³¹=CR³²-O- and - CR³¹=CR³²-S-;

R⁶ is (a) hydrogen, (b) halogen, (c) -(C₁-C₆)alkyl optionally substituted with one to three substituents independently selected from the group consisting of halogen, -OCF₃ and -CF₃, (d) -CN, (e) -OR¹², (f) -trifluoromethyl, (g) -NO₂, (h) -SO₂-R¹³, (i) -C(O)₂R⁹, (j) -C(O)NR¹⁹R²⁰, (k) -C(O)R¹⁶, (l) -NR²¹C(O)NR²¹R²², (m) -NR¹⁹-C(O)R²⁰ or (n) -NR¹⁷R¹⁸;

R⁷ is (a) hydrogen, (b) -(C₁-C₄)alkyl wherein each carbon atom is optionally substituted with 1 to 3 halo atoms or (c) -(CH₂)_nCOOR⁹;

R⁸ is (a) hydrogen, (b) -(C₁-C₆)alkyl, (c) -C(O)-OR⁹, (d) -C(O)NR¹⁰R¹¹ or (e) -CN; provided that in substituent (c), R⁹ is other than methyl or ethyl; and provided that in substituent (d), R¹⁰ and R¹¹ are not both hydrogen;

R⁹ is (a) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (b) -(C₂-C₁₂)alkenyl optionally substituted with phenyl, (c) -(C₂-C₁₂)dialkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R¹⁰ and R¹¹ are independently (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₃-C₁₀)cycloalkyl optionally substituted with one or more substituents independently selected from Group V, (d) -(C₂-C₁₂)alkenyl or (e) -het;

or R¹⁰ and R¹¹ for any occurrence may be taken together with the nitrogen atom to which are they attached to form het;

R¹² is (a) hydrogen or (b) -(C₁-C₆)alkyl wherein each carbon atom is optionally substituted with 1 to 3 fluoro atoms;

R¹³ is (a) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (b) -(C₂-C₁₂)alkenyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -NR¹⁷R¹⁸, (e) -aryl or (f) -het;

R¹⁴ is (a) hydrogen, (b) -(C₁-C₆)alkyl or (c) -O-R³⁴;

R¹⁵ is (a) hydrogen or (b) -(C₁-C₆)alkyl;

or R¹⁴ and R¹⁵ are taken together with the carbon atom to which they are attached to form a carbonyl group;

R¹⁶ is (a) hydrogen, (b) -(C₁-C₆)alkyl wherein each carbon atom is optionally substituted with 1 to 3 fluoro atoms, (c) -(C₀-C₆)alkyl-(C₃-C₁₀)cycloalkyl, (d) -(C₀-C₆)alkyl-aryl or (e) -(C₀-C₆)alkyl-het;

R¹⁷ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -aryl, (d) -het, (e) -OR³⁴ or (f) -(C₃-C₁₀)cycloalkyl;

R¹⁸ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -aryl, (d) -het, (e) -C(O)-R²⁸, (f) -S(O)₂-R²⁹, (g) -OR³⁴ or (h) -(C₃-C₁₀)cycloalkyl;

5 or R¹⁷ and R¹⁸ for any occurrence are taken together with the nitrogen atom to which they are attached to form het;

R¹⁹ and R²⁰ for each occurrence are independently

(a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₀-C₆)alkyl-aryl, (d) -(C₀-C₆)alkyl-het, (e) -C(O)-NR²⁶R²⁷, (f) -C(O)-R²⁸, (g) -S(O)₂-R²⁹, (h) -OR³⁴ or
10 (i) -(C₃-C₁₀)cycloalkyl;

or R¹⁹ and R²⁰ for any occurrence are taken together with the nitrogen atom to which they are attached to form het;

R²¹ and R²² for each occurrence are independently

(a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one to three substituents
15 independently selected from Group V, (c) -aryl, (d) -het, (e) -(C₃-C₁₀)cycloalkyl or (f) -OR³⁴;

or R²¹ and R²² are taken together with the nitrogen atom to which they are attached to form het;

R²³ is (a) hydrogen, (b) -(C₁-C₄)alkyl optionally substituted with one or more
20 substituents independently selected from Group V or (c) -C(O)-R²⁴;

R²⁴ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R²⁵ for each occurrence is independently (a) hydrogen, (b) -(C₁-C₆)alkyl,
25 (c) -COR²⁹ or (d) -SO₂R²⁹;

R²⁶ and R²⁷ for each occurrence are independently (a) hydrogen, (b) -(C₁-C₆)alkyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -(C₀-C₆)alkyl-aryl, or (e) -(C₀-C₆)alkyl-het,

R²⁸ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more
30 substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

R²⁹ is (a) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (b) -(C₂-C₁₂)alkenyl, (c) -(C₃-C₁₀)cycloalkyl, (d) -aryl or (e) -het;

R³⁰ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₁-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -C(O)-R³¹ or (f) -S(O)_m-R³²;

5 R³¹ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl, (f) -het or (g) -OR³⁴;

R³² is (a) hydrogen, (b) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₃-C₁₀)cycloalkyl, (e) -aryl or (f) -het;

10 R³³ is (a) -(C₀-C₆)alkyl-aryl, (b) -(C₀-C₆)alkyl-het, (c) -(C₇-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (d) -(C₁-C₆)alkyl wherein at least one carbon atom is substituted with 1 to 3 fluoro atoms, (e) -(C₂-C₁₂)alkenyl or (f) -(C₃-C₁₀)cycloalkyl;

15 R³⁴ is (a) -aryl, (b) -het, (c) -(C₁-C₁₂)alkyl optionally substituted with one or more substituents independently selected from Group V, (d) -(C₂-C₁₂)alkenyl or (e) -(C₃-C₁₀)cycloalkyl;

20 -(C₃-C₁₀)cycloalkyl for each occurrence is a fully or partially saturated mono-, bi- or tricyclic ring containing three to ten carbon atoms; wherein in the bicyclic ring, a monocyclic cycloalkyl ring is spiro fused to another cycloalkyl ring or is fused via two carbon atoms to a benzene ring or another cycloalkyl ring; and wherein in the tricyclic ring, a bicyclic ring is spiro fused to a cycloalkyl ring or is fused via two atoms to a benzene ring or another cycloalkyl ring;

25 said -(C₃-C₁₀)cycloalkyl optionally contains one to three bridging atoms independently selected from carbon, oxygen, sulfur and nitrogen; said bridging atoms are attached to two carbon atoms in the ring; and said bridging atoms are optionally substituted with one to three groups independently selected from -(C₁-C₆)alkyl and hydroxy;

30 said cycloalkyl ring is optionally substituted on one ring if the moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with one or more substituents independently selected from Group V;

Group V is (a) -(C₁-C₆)alkyl optionally substituted with one or two hydroxy, (b) -(C₂-C₅)alkynyl, (c) -halogen, (d) -NR³⁵R³⁶, (e) -NO₂, (f) -OCF₃, (g) -OR³⁷, (h) -SR³⁷, (i) -oxo, (j) -trifluoromethyl, (k) -CN, (l) -C(O)NR³⁵-OH, (m) -COOR³⁵, (n) -O-

C(O)-(C₁-C₆)alkyl, (o) -(C₃-C₁₀)cycloalkyl optionally substituted with CN, (p) -(C₀-C₆)alkyl-aryl, (q) -(C₀-C₆)alkyl-het, (r) -C(O)-(C₁-C₆)alkyl or (s) -C(O)-aryl;

R³⁵ and R³⁶ for each occurrence are independently (a) hydrogen, (b) -(C₁-C₆)alkyl or (c) -(C₀-C₆)alkyl-aryl;

5 R³⁷ is (a) hydrogen, (b) -(C₁-C₆)alkyl optionally substituted with one or more halo, hydroxy or methoxy, (c) -(C₀-C₆)alkyl-aryl or (d) -(C₀-C₆)alkyl-het;

aryl is (a) phenyl optionally substituted with one or more substituents independently selected from Group Z; (b) naphthyl optionally substituted with one or more substituents independently selected from Group Z or (c) biphenyl optionally substituted with one or more substituents independently selected from Group Z;

10 het for each occurrence is a 4-, 5-, 6-, 7- and 8-membered fully saturated, partially saturated or fully unsaturated mono-, bi- or tricyclic heterocyclic ring containing from one to four heteroatoms independently selected from the group consisting of oxygen, sulfur and nitrogen; wherein in the bicyclic ring, a monocyclic heterocyclic ring is spiro fused to a -(C₃-C₈)cycloalkyl ring or to another heterocyclic ring which is fully or partially saturated; or is fused via two atoms to a benzene ring, a -(C₃-C₈)cycloalkyl ring or another heterocyclic ring; and wherein in the tricyclic ring, a bicyclic ring is spiro fused to a -(C₃-C₈)cycloalkyl ring or to another heterocyclic ring which is fully or partially saturated; or is fused via two atoms to a benzene ring, a (C₃-C₈)cycloalkyl ring, or another heterocyclic ring;

20 said het optionally contains one to three bridging atoms independently selected from oxygen, sulfur and nitrogen; said bridging atoms are attached to two other atoms in the ring; and said bridging atoms are optionally substituted with one to three groups independently selected from -(C₁-C₆)alkyl and hydroxy;

25 said het optionally has one or two oxo groups substituted on carbon or one or two oxo groups substituted on sulfur;

30 said het is optionally substituted on carbon or nitrogen, on one ring if the moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with one or more substituents independently selected from Group Z;

Group Z for each occurrence is independently (a) hydrogen, (b) halogen, (c) trifluoromethyl, (d) hydroxy, (e) -OCF₃, (f) -CN, (g) -NO₂, (h) -(C₁-C₆)alkyl optionally substituted with one or more substituents independently selected from the group consisting of hydroxy, halogen, -OCF₃ and -CF₃, (i) -(C₂-C₆)alkenyl

optionally substituted with phenyl, (j) $-(C_2-C_5)alkynyl$, (k) $-(C_1-C_6)alkoxy$, (l) $-(C_0-C_6)alkyl-phenyl$ optionally substituted with one or more substituents independently selected from the group consisting of halogen, $-OCF_3$, $-CF_3$, $-(C_1-C_4)alkyl$, $-(C_1-C_4)alkoxy$ and $-C(O)CH_3$, (m) $-(C_0-C_6)alkyl-naphthyl$ optionally substituted with one or more substituents independently selected from the group consisting of halogen, $-OCF_3$, $-CF_3$, $-(C_1-C_4)alkyl$, $-(C_1-C_4)alkoxy$ and $-C(O)CH_3$, (n) $-C(O)_2R^{35}$, (o) $-(C_0-C_6)alkyl-C(O)NR^{35}R^{36}$, (p) $-(C_0-C_6)alkyl-C(O)R^{38}$, (q) $-NR^{35}R^{36}$, (r) $-NR^{35}-C(O)NR^{35}R^{36}$, (s) $-NR^{35}-C(O)R^{36}$, (t) $-OR^{37}$, (u) $-SR^{37}$, (v) $-(C_3-C_{10})cycloalkyl$, (w) $-(C_0-C_6)alkyl-pyridinyl$ optionally substituted with one or more $-(C_1-C_6)alkyl$ which is optionally substituted with one or more substituents independently selected from the group consisting of hydroxy and halo, (x) $-(C_0-C_6)alkyl-piperidinyl$ optionally substituted with one or more $-(C_1-C_6)alkyl$ which is optionally substituted with one or more substituents independently selected from hydroxy and halo, (y) $-SO_2-R^{37}$, (z) $-SO_2-NR^{35}R^{36}$ or (a1) $-S-phenyl-CH_2OH$;

R^{38} is (a) $-(C_1-C_6)alkyl$, (b) $-(C_0-C_6)alkyl-phenyl$, (c) $-(C_0-C_6)alkyl-phenanthrenyl$ optionally substituted with one to three CF_3 , (d) $-(C_0-C_6)alkyl-pyrrolidinyl$ or (e) $-(C_0-C_6)alkyl-morpholinyl$;

or any two Z Groups for any occurrence in the same variable may be taken together to form (a) a carbocyclic ring of the formula $-(CH_2)_e-$ or (b) a heterocyclic ring selected from the group consisting of $-O(CH_2)_rO-$, $-(CH_2)_gNH-$ and $-CH=CHNH-$;

m is 0, 1 or 2;

n is 0, 1, 2 or 3;

b is 3, 4, 5, 6 or 7;

c, f, g, j and k are each independently 2, 3, 4, 5 or 6; and

e is 3, 4, 5, 6 or 7;

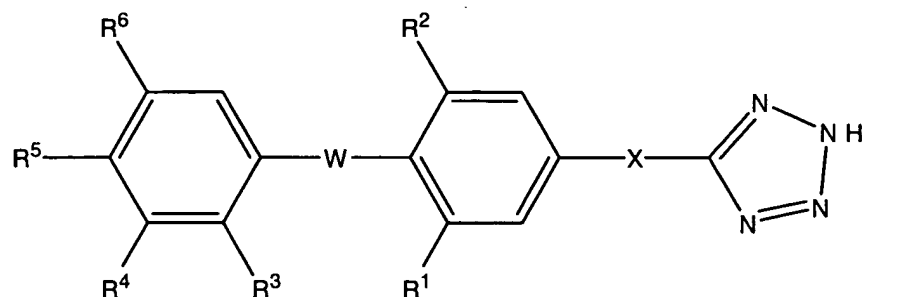
provided that in a compound of the above formula: 1) the substituent $-C(R^{14})(R^{15})(R^{16})$ in R^4 is other than $(C_1-C_4)alkyl$; and 2) R^4 is halo only when R^8 is $-C(O)-OR^9$ or $-C(O)NR^{10}R^{11}$;

and a pharmaceutically acceptable carrier.

25. A composition of claim 24 wherein the compound is selected from the group consisting of:

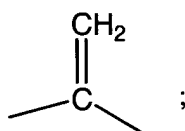
8-[[5-[2,6-dichloro-4-(4,5-dihydro-3,5-dioxo-1,2,4-triazine-2(3H)-yl)phenoxy]-2-hydroxyphenyl]sulfonyl]-spiro[8-azabicyclo[3.2.1]octane-3,2'-(3'H)-dihydro-furan];

- 2-{3,5-dichloro-4-[3-(3,3-dimethyl-piperidine-1-sulfonyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;
- 2-{3,5-dichloro-4-[4-hydroxy-3-(3-methyl-3-phenyl-piperidine-1-sulfonyl)-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;
- 5 N-cyclohexyl-5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-2-hydroxy-benzenesulfonamide;
- N-bicyclo[2.2.1]hept-2-yl-5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-2-hydroxy-benzamide;
- 2-{3,5-dichloro-4-[3-(3,3-dimethyl-piperidine-1-carbonyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;
- 10 N-bicyclo[2.2.1]hept-2-yl-5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-2-hydroxy-benzamide;
- 2-{3,5-dichloro-4-[4-hydroxy-3-(3-methyl-3-phenyl-piperidine-1-carbonyl)-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;
- 15 5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-N-(6,6-dimethyl-bicyclo[3.1.1]hept-2-yl)-2-hydroxy-benzamide;
- 2-{3,5-dichloro-4-[3-(3,5-dimethyl-piperidine-1-carbonyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;
- 2-{3,5-dichloro-4-[4-hydroxy-3-(piperidine-1-carbonyl)-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;
- 20 N-cyclohexyl-5-[2,6-dichloro-4-(3,5-dioxo-4,5-dihydro-3H-[1,2,4]triazin-2-yl)-phenoxy]-2-hydroxy-benzamide;
- 2-{3,5-dichloro-4-[3-(3,4-dihydro-1H-isoquinoline-2-carbonyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione;
- 25 2-{4-[3-(4-fluoro-benzyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-2H-[1,2,4]triazine-3,5-dione; and
- 2-{3,5-dichloro-4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-phenyl}-2H-[1,2,4]triazine-3,5-dione.
26. A topical pharmaceutical composition for increasing the rate of nail
- 30 growth which comprises an effective amount of a compound of the formula



or a stereoisomer, a pharmaceutically acceptable salt or prodrug thereof, or a pharmaceutically acceptable salt of the prodrug, wherein:

W is O, S, SO, SO₂, CH₂, CF₂, CHF, C(=O), CH(OH), NR^a, or



5

X is O, CH₂, CH₂CH₂, S, SO, SO₂, CH₂NR^a, NR^a, or a bond;

each R^a is independently hydrogen, C₁-C₆alkyl, or C₁-C₆alkyl substituted with one substituent selected from C₃-C₆cycloalkyl or methoxy;

10 R¹, R², R³ and R⁶ are independently hydrogen, halogen, C₁-C₈alkyl, -CF₃, -OCF₃, -OC₁-C₈alkyl, or -CN;

R⁴ is hydrogen, C₁-C₁₂alkyl, [C₁-C₁₂alkyl that is substituted with from one to three substituents independently selected from Group V], C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, halogen, -CN, -OR^b, -SR^c, -S(=O)R^c, -S(=O)₂R^c, aryl, heteroaryl, 15 C₃-C₁₀ cycloalkyl, heterocycloalkyl, -S(=O)₂NR^cR^d, -C(=O)NR^cR^d, -C(=O)OR^c, -NR^aC(=O)R^d, -NR^aC(=O)NR^cR^d, -NR^aS(=O)₂R^d, -NR^aR^d, -C(=O)R^c,

or R³ and R⁴ may be taken together with the carbon atoms to which they are attached to form an unsubstituted or substituted carbocyclic ring of formula -(CH₂)_i- or an unsubstituted or substituted heterocyclic ring selected from the group 20 consisting of -Q-(CH₂)_j- and -(CH₂)_k-Q-(CH₂)_l- wherein Q is O, S or NR^a; i is 3, 4, 5, 6 or 7; j is 2, 3, 4, 5, or 6; k and l are each independently 1, 2, 3, 4, or 5, and any substituents up to four are selected from C₁-C₄alkyl, -OR^b, oxo, -CN, phenyl, or -NR^aR^g;

25 R^b is hydrogen, C₁-C₁₂alkyl, [C₁-C₁₂alkyl substituted with one to three substituents independently selected from Group V], aryl, heteroaryl, C₃-C₁₀ cycloalkyl, heterocycloalkyl, -C(=O)NR^cR^d, or -C(=O)R^f;

R^c and R^d are each independently selected from hydrogen, C_1 - C_{12} alkyl, [C_1 - C_{12} alkyl substituted with one to three substituents independently selected from Group VI], C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, aryl, heteroaryl, C_3 - C_{10} cycloalkyl, heterocycloalkyl,

5 or R^c and R^d may together along with the atom(s) to which they are attached form a 3-10 membered unsubstituted or substituted heterocyclic ring, which may contain a second heterogroup selected from O, NR^e , or S, wherein any substituents up to four are selected from C_1 - C_4 alkyl, $-OR^b$, oxo, -CN, phenyl, or - NR^aR^g ;

10 R^5 is -OH, $-OC_1$ - C_6 alkyl, $-OC(=O)R^f$, -F, $-C(=O)OR^c$,

or R^4 and R^5 may together with the atom(s) to which they are attached form a heterocyclic ring selected from the group consisting of $-CR^c=CR^a-NH-$, $-N=CR^a-NH-$, $-CR^c=CR^a-O-$, $-CR^c=CR^a-S-$, $-CR^c=N-NH-$, or $-CR^a=CR^a-CR^a=N-$;

Group V is halogen, $-CF_3$, $-OCF_3$, hydroxy, oxo, C_1 - C_6 alkoxy, -CN, aryl, 15 heteroaryl, C_3 - C_{10} cycloalkyl, heterocycloalkyl, $-SR^f$, $-S(=O)R^f$, $-S(=O)_2R^f$, $[-S(=O)_2NR^aR^f]$, wherein R^a and R^f may together along with the atom(s) to which they are attached form a 3-8 membered heterocyclic ring, which may contain a second heterogroup selected from O, NR^e or S], $-NR^aR^g$, or $[-C(=O)NR^aR^f]$, wherein R^a and R^f may together along with the atom(s) to which they are attached 20 form a 3-8 membered heterocyclic ring, which may contain a second heterogroup selected from O, NR^e or S];

Group VI is halogen, hydroxy, oxo, C_1 - C_6 alkoxy, aryl, heteroaryl, C_3 - C_8 cycloalkyl, heterocycloalkyl, -CN, or $-OCF_3$;

R^e is hydrogen, -CN, C_1 - C_{10} alkyl, [C_1 - C_{10} alkyl substituted with one to three 25 substituents independently selected from Group V], C_2 - C_{10} alkenyl, C_2 - C_{10} alkoxy, C_3 - C_{10} cycloalkyl, aryl, heteroaryl, $-C(=O)R^f$, $-C(=O)OR^f$, $-C(=O)NR^aR^f$, $-S(=O)_2NR^aR^f$, or $-S(=O)_2R^f$;

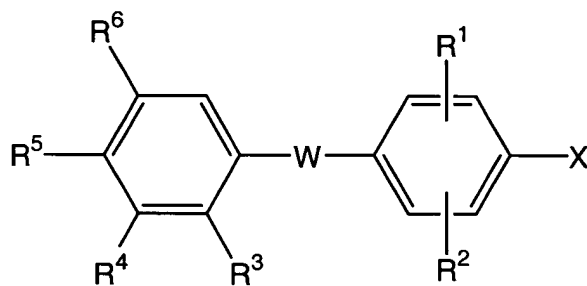
R^f is hydrogen, C_1 - C_{10} alkyl, [C_1 - C_{10} alkyl substituted with from one to three 30 substituents selected from Group VI], C_2 - C_{10} alkenyl, C_2 - C_{10} alkoxy, C_3 - C_{10} cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; and

R^g is hydrogen, C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, C_2 - C_6 alkenyl, aryl, $-C(=O)R^f$, $-C(=O)OR^f$, $-C(=O)NR^aR^f$, or $-S(=O)_2R^f$, provided that R^1 and R^2 are not both hydrogen, further provided that when X is CH_2 , W is NR^a , R^3 is hydrogen and R^5 is

-OH, then R^6 and R^4 are not both $-C(CH_3)_3$, further provided that when X is CH_2 or CH_2CH_2 , W is O, and R^3 and R^6 are hydrogen, then R^4 is not halogen, $-CF_3$, C_1 - C_6 alkyl or C_3 - C_7 cycloalkyl, and further provided that when R^3 and R^4 are hydrogen and W is O then R^6 is not halogen, $-CF_3$, C_1 - C_6 alkyl or C_3 - C_7 cycloalkyl;

5 and a pharmaceutically acceptable carrier.

27. A topical pharmaceutical composition for increasing the rate of nail growth which comprises an effective amount of a compound of the formula



a stereoisomer or prodrug thereof, or a pharmaceutically acceptable salt of
10 said compound, stereoisomer, or prodrug, wherein:

W is oxygen, sulfur, $-SO-$, $-S(O)_2-$, $-CH_2-$, $-CF_2-$, $-CHF-$, $-C(O)-$, $-CH(OH)-$, $-NR^a$, or $-C(=CH_2)-$;

R^1 , R^2 , R^3 , and R^6 are each independently hydrogen, halogen, $-(C_1-C_8)$ alkyl, $-CF_3$, $-OCF_3$, $-O(C_1-C_8)$ alkyl, or $-CN$;

15 R^4 is hydrogen, $-(C_1-C_{12})$ alkyl substituted with zero to three substituents independently selected from Group V, $-(C_2-C_{12})$ alkenyl, $-(C_2-C_{12})$ alkynyl, halogen, $-CN$, $-OR^b$, $-SR^c$, $-S(O)R^c$, $-S(O)_2R^c$, aryl, heteroaryl, $-(C_3-C_{10})$ cycloalkyl, heterocycloalkyl, $-S(O)_2NR^cR^d$, $-C(O)NR^cR^d$, $-C(O)OR^c$, $-NR^aC(O)R^d$, $-NR^aC(O)NR^cR^d$, $-NR^aS(O)_2R^d$, or $-C(O)R^c$; or

20 R^3 and R^4 are taken together along with the carbon atoms to which they are attached to form a carbocyclic ring of formula $-(CH_2)_i-$ or a heterocyclic ring of formula $-(CH_2)_k-Q-(CH_2)_l-$ wherein Q is oxygen, sulfur, or $-NR^e$; i is 3, 4, 5, or 6; k is 0, 1, 2, 3, 4, or 5; and l is 0, 1, 2, 3, 4, or 5; and wherein said carbocyclic ring and said heterocyclic ring are each substituted with zero to four substituents

25 independently selected from $-(C_1-C_4)$ alkyl, $-OR^b$, oxo, $-CN$, phenyl, or $-NR^aR^g$;

R^5 is hydroxy, $-O(C_1-C_6)$ alkyl, $-OC(O)R^f$, fluorine, or $-C(O)OR^c$; or

R^4 and R^5 are taken together along with the carbon atoms to which they are attached to form a heterocyclic ring selected from the group consisting of -

$\text{CR}^c=\text{CR}^a\text{-NH-}$, $\text{-N=CR}^a\text{-NH-}$, $\text{-CR}^c=\text{CR}^a\text{-O-}$, $\text{-CR}^c=\text{CR}^a\text{-S-}$, $\text{-CR}^c=\text{N-NH-}$, and $\text{-CR}^a=\text{CR}^a\text{-CR}^a=\text{N-}$;

R^a for each occurrence is independently hydrogen, or $\text{-(C}_1\text{-C}_6\text{)alkyl}$ substituted with zero or one $\text{-(C}_3\text{-C}_6\text{)cycloalkyl}$ or methoxy;

- 5 R^b for each occurrence is independently hydrogen, $\text{-(C}_1\text{-C}_{12}\text{)alkyl}$ substituted with zero to three substituents independently selected from Group V, aryl, heteroaryl, $\text{-(C}_3\text{-C}_{10}\text{)cycloalkyl}$, heterocycloalkyl, $\text{-C(O)NR}^c\text{R}^d$, or -C(O)R^f ;

- R^c and R^d for each occurrence are each independently hydrogen, $\text{-(C}_1\text{-C}_{12}\text{)alkyl}$ substituted with zero to three substituents independently selected from
10 Group VI, $\text{-(C}_2\text{-C}_{12}\text{)alkenyl}$, $\text{-(C}_2\text{-C}_{12}\text{)alkynyl}$, aryl, heteroaryl, $\text{-(C}_3\text{-C}_{10}\text{)cycloalkyl}$, or heterocycloalkyl;

provided that when R^d is the moiety -SR^c , -S(O)R^c , or $\text{-S(O)}_2\text{R}^c$, R^c is other than hydrogen; or

- R^c and R^d are taken together along with the atom(s) to which they are
15 attached to form a 3-10 membered heterocyclic ring which may optionally contain a second heterogroup selected from oxygen, -NR^e -, or sulfur; and wherein said heterocyclic ring is substituted with zero to four substituents independently selected from $\text{-(C}_1\text{-C}_4\text{)alkyl}$, -OR^b , oxo, -CN , phenyl, or $\text{-NR}^a\text{R}^g$;

- R^e for each occurrence is hydrogen, -CN , $\text{-(C}_1\text{-C}_{10}\text{)alkyl}$ substituted with zero
20 to three substituents independently selected from Group V, $\text{-(C}_2\text{-C}_{10}\text{)alkenyl}$, $\text{-(C}_2\text{-C}_{10}\text{)alkoxy}$, $\text{-(C}_3\text{-C}_{10}\text{)cycloalkyl}$, aryl, heteroaryl, -C(O)R^f , -C(O)OR^f , $\text{-C(O)NR}^a\text{R}^f$, or $\text{-S(O)}_2\text{R}^f$;

- R^f for each occurrence is independently $\text{-(C}_1\text{-C}_{10}\text{)alkyl}$ substituted with zero to three substituents independently selected from Group VI, $\text{-(C}_2\text{-C}_{12}\text{)alkenyl}$, $\text{-(C}_2\text{-C}_{10}\text{)alkynyl}$, $\text{-(C}_3\text{-C}_{10}\text{)cycloalkyl}$, aryl, heteroaryl, or heterocycloalkyl;
25

R^g for each occurrence is independently hydrogen, $\text{-(C}_1\text{-C}_6\text{)alkyl}$, $\text{-(C}_2\text{-C}_6\text{)alkenyl}$, aryl, -C(O)R^f , -C(O)OR^f , $\text{-C(O)NR}^a\text{R}^f$, $\text{-S(O)}_2\text{R}^f$, or $\text{-(C}_3\text{-C}_8\text{)cycloalkyl}$;

- Group V is halogen, -CF_3 , -OCF_3 , -OH , oxo, $\text{-(C}_1\text{-C}_6\text{)alkoxy}$, -CN , aryl, heteroaryl, $\text{-(C}_3\text{-C}_{10}\text{)cycloalkyl}$, heterocycloalkyl, -SR^f , -S(O)R^f , $\text{-S(O)}_2\text{R}^f$, $\text{-S(O)}_2\text{NR}^a\text{R}^f$, $\text{-NR}^a\text{R}^g$, or $\text{-C(O)NR}^a\text{R}^f$;
30

Group VI is halogen, hydroxy, oxo, $\text{-(C}_1\text{-C}_6\text{)alkoxy}$, aryl, heteroaryl, $\text{-(C}_3\text{-C}_8\text{)cycloalkyl}$, heterocycloalkyl, -CN , or -OCF_3 ;

provided that when R^d is $\text{-(C}_1\text{-C}_{12}\text{)alkyl}$ substituted with zero to three substituents independently selected from Group V, wherein said Group V

substituent is oxo, said oxo group is substituted on a carbon atom other than the C₁ carbon atom in -(C₁-C₁₂)alkyl;

aryl for each occurrence is independently phenyl or naphthyl substituted with zero to four substituents independently selected from halogen, -(C₁-C₆)alkyl, -CN, -SR^f, -S(O)R^f, -S(O)₂R^f, -(C₃-C₆)cycloalkyl, -S(O)₂NR^aR^f, -NR^aR^g, -C(O)NR^aR^f, -OR^b,
5 -perfluoro-(C₁-C₄)alkyl, or -COOR^f;

provided that when said substituent(s) on aryl are -SR^f, -S(O)R^f, -S(O)₂R^f, -S(O)₂NR^aR^f, -NR^aR^g, -C(O)NR^aR^f, -OR^b, or -COOR^f, said substituents R^b, R^f, and R^g, are other than aryl or heteroaryl;

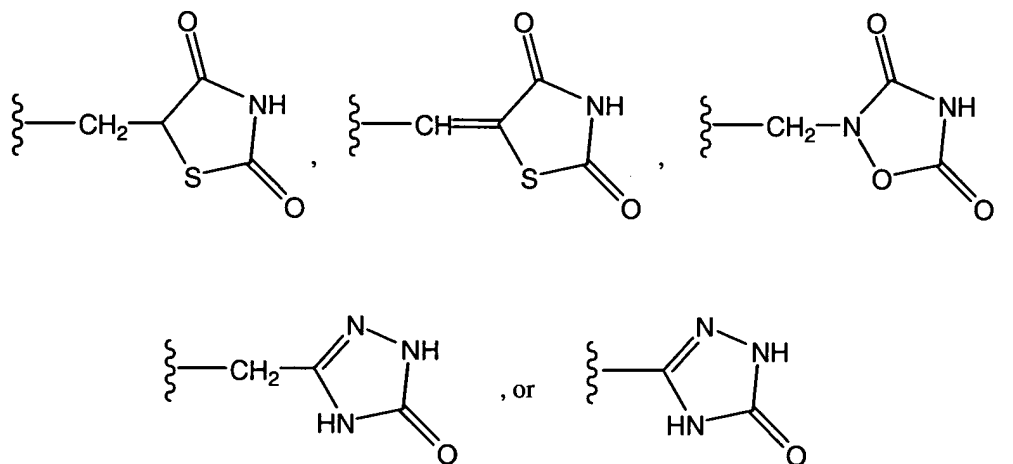
10 heteroaryl for each occurrence is independently a 5-, 6-, 7-, 8-, or 9-membered monocyclic or bicyclic ring having from one to three heteroatoms selected from O, N, or S;

wherein in said bicyclic ring, a monocyclic heteroaryl ring is fused to a benzene ring or to another heteroaryl ring, and having zero to three substituents
15 independently selected from halogen, -(C₁-C₄)alkyl, -CF₃, -OR^b, -NR^aR^g, or -COOR^f;

provided that when said substituent(s) on heteroaryl are -NR^aR^g, -OR^b, or -COOR^f, said substituents R^b, R^f, and R^g, are other than aryl or heteroaryl;

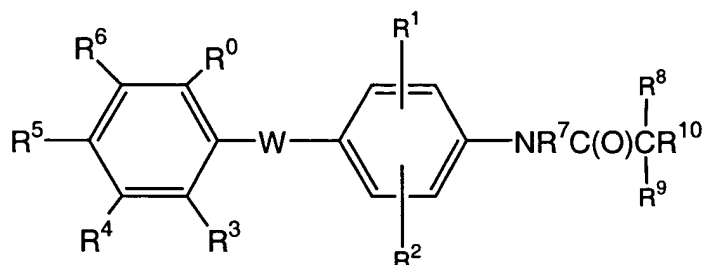
heterocycloalkyl for each occurrence is independently a 5-, 6-, 7-, 8-, or 9-membered monocyclic or bicyclic cycloalkyl ring having from one to three
20 heteroatoms selected from oxygen, -NR^g, or sulfur, and having zero to four substituents independently selected from -(C₁-C₄)alkyl, -OR^b, oxo, -CN, phenyl, or -NR^aR^g; and

X is

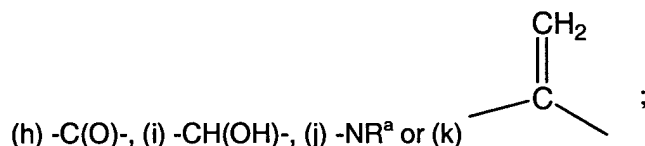


25 and a pharmaceutically acceptable carrier.

28. A topical pharmaceutical composition for increasing the rate of nail growth which comprises an effective amount of a compound of the formula



- 5 an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug; wherein W is (a) -O-, (b) -S-, (c) -SO-, (d) -SO₂-, (e) -CH₂-, (f) -CF₂-, (g) -CHF-,



- ¹⁰ R⁰ is (a) hydrogen, (b) -(C₁-C₆)alkyl substituted with zero or one substituent selected from the group consisting of (1) -(C₃-C₆)cycloalkyl, (2) heterocycloalkyl and (3) phenyl substituted with zero or one substituent selected from the group consisting of (i) -(C₁-C₄)alkyl, (ii) halogen, (iii) -CF₃ and (iv) -OCF₃; (c) -C(O)R^h, (d) -S(O)₂R^h or (e) halogen;

- ¹⁵ R¹, R², R³ and R⁶ are each independently (a) hydrogen, (b) halogen, (c) -(C₁-C₈)alkyl, (d) -CF₃, (e) -OCF₃, (f) -O(C₁-C₈)alkyl, or (g) -CN;

- ²⁰ R⁴ is (a) hydrogen, (b) -(C₁-C₁₂)alkyl substituted with zero to three substituents independently selected from Group V, (c) -(C₂-C₁₂)alkenyl, (d) -(C₂-C₁₂)alkynyl, (e) halogen, (f) -CN, (g) -OR^b, (h) -SR^c, (i) -S(O)R^c, (j) -S(O)₂R^c, (k) aryl, (l) heteroaryl, (m) -(C₃-C₁₀)cycloalkyl, (n) heterocycloalkyl, (o) -S(O)₂NR^cR^d, (p) -C(O)NR^cR^d, (q) -C(O)OR^c, (r) -NR^aC(O)R^d, (s) -NR^aC(O)NR^cR^d, (t) -NR^aS(O)₂R^d, (u) -NR^aR^d or (v) -C(O)R^c;

- ²⁵ or R³ and R⁴ are taken together along with the carbon atoms to which they are attached to form a carbocyclic ring of formula -(CH₂)_i- or a heterocyclic ring of formula -(CH₂)_k-Q-(CH₂)_i- wherein Q is -O-, -S- or -NR^e-; i is 3, 4, 5 or 6; k is 0, 1, 2, 3, 4 or 5; and l is 0, 1, 2, 3, 4 or 5; and wherein the carbocyclic ring and the heterocyclic ring are each substituted with zero to four substituents independently selected from (a) -(C₁-C₄)alkyl, (b) -OR^b, (c) oxo, (d) -CN, (e) phenyl or (f) -NR^aR^g;

- R^5 is (a) -OH, (b) $-O(C_1-C_6)alkyl$, (c) $-OC(O)R^f$, (d) F, or (e) $-C(O)OR^c$;
or R^4 and R^5 are taken together along with the carbon atoms to which they
are attached to form a heterocyclic ring selected from the group consisting of –
 $CR^c=CR^a-NH-$, $-N=CR^a-NH-$, $-CR^c=CR^a-O-$, $-CR^c=CR^a-S-$, $-CR^c=N-NH-$ and –
5 $CR^a=CR^a-CR^a=N-$;
 R^7 is (a) hydrogen or (b) $-(C_1-C_6)alkyl$;
 R^8 and R^9 are each independently (a) hydrogen, (b) $-(C_1-C_6)alkyl$, (c) aryl, or
(d) halogen;
 R^{10} is (a) $-(C_0-C_1)alkyl-C(O)OH$, (b) $-(C_0-C_1)alkyl-C(O)OR^f$, (c) $-(C_0-C_1)alkyl-$
10 $C(O)NR^cR^d$, or (d) $-(C_0-C_1)alkyl-OH$;
 R^a for each occurrence is independently (a) hydrogen or (b) $-(C_1-C_6)alkyl$
substituted with zero or one $-(C_3-C_6)cycloalkyl$ or methoxy;
 R^b for each occurrence is independently (a) hydrogen, (b) $-(C_1-C_{12})alkyl$
substituted with zero to three substituents independently selected from Group V, (c)
15 aryl, (d) heteroaryl, (e) $-(C_3-C_{10})cycloalkyl$, (f) heterocycloalkyl, (g) $-C(O)NR^cR^d$, or (h)
 $-C(O)R^f$;
 R^c and R^d for each occurrence are each independently (a) hydrogen, (b) $-(C_1-$
 $C_{12})alkyl$ substituted with zero to three substituents independently selected from
Group VI, (c) $-(C_2-C_{12})alkenyl$, (d) $-(C_2-C_{12})alkynyl$, (e) aryl, (f) heteroaryl, (g) $-(C_3-$
20 $C_{10})cycloalkyl$ or (h) heterocycloalkyl;
provided that when R^4 is the moiety $-SR^c$, $-S(O)R^c$ or $-S(O)_2R^c$, R^c is other
than hydrogen;
or R^c and R^d are taken together along with the atom(s) to which they are
attached to form a 3-10 membered heterocyclic ring which may optionally contain a
25 second heterogroup selected from -O-, $-NR^e$ - or $-S-$; and wherein the heterocyclic
ring is substituted with zero to four substituents independently selected from (a) $-(C_1-$
 $C_4)alkyl$, (b) $-OR^b$, (c) oxo, (d) -CN, (e) phenyl or (f) $-NR^aR^g$;
 R^e for each occurrence is (a) hydrogen, (b) -CN, (c) $-(C_1-C_{10})alkyl$ substituted
with zero to three substituents independently selected from Group V, (d) $-(C_2-$
30 $C_{10})alkenyl$, (e) $-(C_2-C_{10})alkoxy$, (f) $-(C_3-C_{10})cycloalkyl$, (g) aryl, (h) heteroaryl, (i) -
 $C(O)R^f$, (j) $-C(O)OR^f$, (k) $-C(O)NR^aR^f$ or (l) $-S(O)_2R^f$;
 R^f for each occurrence is independently (a) $-(C_1-C_{10})alkyl$ substituted with zero
to three substituents independently selected from the Group VI, (b) $-(C_2-C_{10})alkenyl$,

(c) $-(C_2-C_{10})$ alkynyl, (d) $-(C_3-C_{10})$ cycloalkyl, (e) aryl, (f) heteroaryl or (g) heterocycloalkyl;

R^g for each occurrence is independently (a) hydrogen, (b) $-(C_1-C_6)$ alkyl, (c) $-(C_2-C_6)$ alkenyl, (d) aryl, (e) $-C(O)R^f$, (f) $-C(O)OR^f$, (g) $-C(O)NR^aR^f$, (h) $-S(O)_2R^f$ or (i) $-(C_3-C_8)$ cycloalkyl;

R^h is (a) $-(C_1-C_6)$ alkyl substituted with zero or one substituent selected from the group consisting of (1) $-(C_3-C_6)$ cycloalkyl, (2) heterocycloalkyl and (3) phenyl substituted with zero or one substituent selected from the group consisting of (i) $-(C_1-C_4)$ alkyl, (ii) halogen, (iii) $-CF_3$ and (iv) $-OCF_3$; (b) phenyl substituted with zero to two substituents independently selected from the group consisting of (1) $-(C_1-C_4)$ alkyl, (2) halogen, (3) $-CF_3$ and (4) $-OCF_3$; (c) $-(C_3-C_6)$ cycloalkyl or (d) heterocycloalkyl;

Group V is (a) halogen, (b) $-CF_3$, (c) $-OCF_3$, (d) $-OH$, (e) $-oxo$, (f) $-(C_1-C_6)$ alkoxy, (g) $-CN$, (h) aryl, (i) heteroaryl, (j) $-(C_3-C_{10})$ cycloalkyl, (k) heterocycloalkyl, (l) $-SR^f$, (m) $-S(O)R^f$, (n) $-S(O)_2R^f$, (o) $-S(O)_2NR^aR^f$ (p) $-NR^aR^g$ or (q) $-C(O)NR^aR^f$;

Group VI is (a) halogen, (b) hydroxy, (c) oxo, (d) $-(C_1-C_6)$ alkoxy, (e) aryl, (f) heteroaryl, (g) $-(C_3-C_8)$ cycloalkyl, (h) heterocycloalkyl, (i) $-CN$, or (j) $-OCF_3$;

provided that when the substituent R^4 is $-(C_1-C_{12})$ alkyl substituted with zero to three substituents independently selected from Group V wherein the Group V substituent is oxo, the oxo group is substituted on a carbon atom other than the C_1 carbon atom in $-(C_1-C_{12})$ alkyl;

aryl for each occurrence is independently phenyl or naphthyl substituted with zero to four substituents independently selected from (a) halogen, (b) $-(C_1-C_6)$ alkyl, (c) $-CN$, (d) $-SR^f$, (e) $-S(O)R^f$, (f) $-S(O)_2R^f$, (g) $-(C_3-C_6)$ cycloalkyl, (h) $-S(O)_2NR^aR^f$, (i) $-NR^aR^g$, (j) $-C(O)NR^aR^f$, (k) $-OR^b$, (l) $-perfluoro-(C_1-C_4)alkyl$, or (m) $-COOR^f$;

provided that when the substituent(s) on aryl are $-SR^f$, $-S(O)R^f$, $-S(O)_2R^f$, $-S(O)_2NR^aR^f$, $-NR^aR^g$, $-C(O)NR^aR^f$, $-OR^b$, or $-COOR^f$, the substituents R^b , R^f and R^g are other than aryl or heteroaryl;

heteroaryl for each occurrence is independently a 5-, 6-, 7-, 8-, 9- or 10-membered monocyclic or bicyclic ring having from 1 to 3 heteroatoms selected from O, N or S; wherein in the bicyclic ring, a monocyclic heteroaryl ring is fused to a benzene ring or to another heteroaryl ring; and having zero to three substituents independently selected from (a) halogen, (b) $-(C_1-C_4)$ alkyl, (c) $-CF_3$, (d) $-OR^b$, (e) $-NR^aR^g$, or (f) $-CO_2R^f$;

provided that when the substituent(s) on heteroaryl are $-OR^b$, $-NR^aR^g$ or

-CO₂R^f, the substituents R^b, R^f and R^g are other than aryl or heteroaryl;

heterocycloalkyl for each occurrence is independently a 4-, 5-, 6-, 7-, 8-, 9- or 10-membered monocyclic or bicyclic cycloalkyl ring having from 1 to 3 heteroatoms selected from O, NR^g or S; and having zero to four substituents independently

- 5 selected from (a) -(C₁-C₄)alkyl, (b) -OR^b, (c) oxo, (d) -CN, (e) phenyl or (f) -NR^aR^g; and a pharmaceutically acceptable carrier.

29. A composition of claim 28 wherein the compound is selected from the group of:

- 10 N-{4-[3-(cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-malonamic acid;
- N-{3-chloro-4-[4-hydroxy-3-(1-isopropyl-2-methyl-propylcarbamoyl)-phenoxy]-5-methyl-phenyl}-malonamic acid;
- N-{3,5-dichloro-4-[3-((1S)-cyclohexyl-ethylcarbamoyl)-4-hydroxy-phenoxy]-phenyl}-malonamic acid;
- 15 N-[3,5-dichloro-4-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-malonamic acid;
- N-[3,5-dichloro-4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-phenyl]-malonamic acid;
- N-[3-chloro-4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- 20 N-[4-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[4-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- 25 N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- N-[3-chloro-4-(3-cyclopropylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- N-[3,5-dichloro-4-(3-cyclopropylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-malonamic acid;
- 30 N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[3,5-dichloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-phenyl]-malonamic acid;

- N-[4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-2-methyl-malonamic acid;
- 5 N-[3-chloro-4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-2-methyl-malonamic acid;
- 10 N-[3-chloro-4-(3-cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;
- N-[4-(3-cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl]-malonamic acid;
- 15 N-[3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl]-malonamic acid;
- N-[4-[3-(4-fluoro-benzoyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl]-malonamic acid;
- 20 N-[4-(3-cyclopentylacetyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;
- N-[4-[3-[(4-fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl]-malonamic acid;
- N-[4-[3-(2-cyclopentyl-1-hydroxy-ethyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl]-malonamic acid;
- 25 N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid methyl ester;
- N-[3-chloro-4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid ethyl ester;
- N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid ethyl ester;
- 30 N-[4-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid methyl ester;
- N-[3-chloro-4-(3-cyclopentanesulfonyl-4-hydroxy-phenoxy)-5-methyl-phenyl]-malonamic acid;

N-[4-(3-cyclopentanesulfonyl-4-hydroxy-phenoxy)-3,5-dimethyl-phenyl]-malonamic acid;

N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-malonamic acid;

5 N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-malonamic acid methyl ester;

N-{3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl}-malonamic acid methyl ester;

10 N-{3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl}-malonamic acid ethyl ester;

N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-2-methyl-malonamic acid methyl ester;

N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-2-methyl-malonamic acid;

15 N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-2-methyl-malonamic acid methyl ester;

N-{3-chloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-5-methyl-phenyl}-2-methyl-malonamic acid;

20 N-{3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl}-2-methyl-malonamic acid methyl ester; and

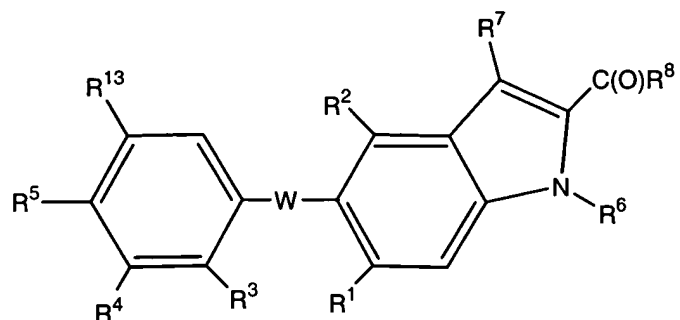
N-{3,5-dichloro-4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-phenyl}-2-methyl-malonamic acid;

N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-malonamic acid; and

25 N-{4-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,5-dimethyl-phenyl}-malonamic acid methyl ester; or an isomer thereof, a prodrug of said compound or isomer, or a pharmaceutically acceptable salt of said compound, isomer or prodrug.

30. A topical pharmaceutical composition for increasing the rate of nail growth which comprises an effective amount of a compound of the formula

30



or the pharmaceutically acceptable salt thereof; wherein

W is oxygen, CH₂, CF₂, NR¹², S(O)_m wherein m is 0, 1 or 2;

5 R¹, R², and R³ are each independently selected from the group consisting of hydrogen, halo, cyano, trifluoromethyl, trifluomethoxy and (C₁-C₆)alkyl;

R⁴ is hydrogen, halo, cyano, (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, (C₃-C₁₀)cycloalkyl, (C₃-C₁₀)cycloalkyl(C₁-C₆)alkyl, (C₆-C₁₀)aryl, (C₆-C₁₀)aryl(C₁-C₆)alkyl, (C₂-C₉)heteroaryl, (C₂-C₉)heteroaryl(C₁-C₆)alkyl, (C₂-C₉)heterocycloalkyl, (C₂-C₉)heterocycloalkyl(C₁-C₆)alkyl, -OR⁹, -S(O)₂NR¹⁰R¹¹, -C(O)NR¹⁰R¹¹, -C(O)R¹⁰, -CH(OH)R¹⁰, -NR¹²C(O)R¹⁰, -NR¹²C(O)NR¹⁰R¹¹, -NR¹²S(O)₂R¹⁰ or -S(O)_nR¹⁰ wherein n is 0, 1 or 2;

R⁵ is hydroxy, fluoro, (C₁-C₄)alkoxy or -OC(O)R¹⁰;

R⁶ is hydrogen, -C(O)CH₃ or (C₁-C₆)alkyl;

15 R⁷ is hydrogen or (C₁-C₆)alkyl;

R⁸ is OR¹² or NR⁹R¹²;

R⁹ for each occurrence is independently hydrogen, (C₁-C₁₂)alkyl, (C₃-C₁₀)cycloalkyl, (C₂-C₉)heterocycloalkyl, (C₆-C₁₀)aryl or (C₂-C₉)heteroaryl;

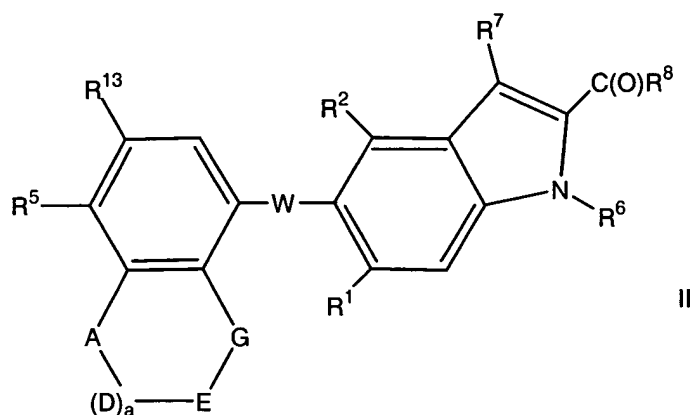
20 R¹⁰ for each occurrence is independently hydrogen, (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, (C₃-C₁₀)cycloalkyl, (C₃-C₉)cycloalkyl(C₁-C₆)alkyl, (C₆-C₁₀)aryl, (C₂-C₉)heteroaryl or halo(C₆-C₁₀)aryl;

R¹¹ for each occurrence is independently hydrogen, (C₁-C₆)alkyl, (C₃-C₁₀)cycloalkyl or (C₃-C₉)cycloalkyl(C₁-C₆)alkyl;

25 or R¹⁰ and R¹¹ may be taken together with the nitrogen to which they are attached to form a 3 to 10 membered heterocyclic group which may contain a second heteroatom selected from oxygen, sulfur or NR¹⁴ wherein R¹⁴ is hydrogen or (C₁-C₆)alkyl;

R¹² for each occurrence is independently hydrogen or (C₁-C₆)alkyl;

R^{13} is hydrogen, halo or (C_1-C_6) alkyl;
 or R^3 and R^4 may be taken together with the carbons to which they are
 attached to form a compound of the formula



II

5 wherein a is 0, 1, 2 or 3;

A, D, E and G are each independently selected from the group consisting of
 $CR^{16}R^{17}$, NR^{18} , oxygen or sulfur;

R^{16} and R^{17} for each occurrence are each independently selected from
 hydrogen or (C_1-C_6) alkyl; and

10 R^{18} is hydrogen, (C_1-C_6) alkyl, $-C(O)R^{10}$ or $-S(O)_2R^{10}$ wherein R^{10} is defined as
 above;

and a pharmaceutically acceptable carrier.

31. A composition according to claim 30 wherein the compound is selected
 from the group consisting of:

15 5-(4-Hydroxy-3-isopropyl-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
 4,6-Dichloro-5-(4-hydroxy-3-isopropyl-phenoxy)-1H-indole-2-carboxylic acid;
 5-(3-sec-butyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
 5-[3-(4-Fluoro-benzyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-
 carboxylic acid;

20 5-{3-[(4-Fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy}-4,6-dimethyl-1H-
 indole-2-carboxylic acid;

5-[3-(2-Cyclopentyl-1-hydroxy-ethyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-
 indole-2-carboxylic acid;

25 5-[3-(4-Fluoro-benzoyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-
 carboxylic acid;

- 5-[3-(Cyclobutyl-methyl-carbamoyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 5-(3-Cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 5 4,6-Dichloro-5-(3-cyclobutylmethanesulfonyl-4-hydroxy-phenoxy)-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-(4-hydroxy-3-isopropyl-phenoxy)-1-methyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-(4-hydroxy-3-isopropyl-phenoxy)-3-methyl-1H-indole-2-carboxylic acid;
- 10 5-[3-(4-Fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 5-[3-(4-Fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-3,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 15 4,6-Dichloro-5-(3-cyclobutylsulfamoyl-4-hydroxy-phenoxy)-1H-indole-2-carboxylic acid;
- 4-Chloro-5-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-5-methyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-[4-hydroxy-3-(1-isopropyl-2-methyl-propylcarbamoyl)-phenoxy]-1H-indole-2-carboxylic acid;
- 20 5-[3-(4-Fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-1,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 5-[3-[(4-Fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy]-3,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 25 5-[3-(4-Fluoro-benzyl)-4-hydroxy-phenoxy]-3,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 5-(3-Cyclopentylmethanesulfonyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-(3-cyclopropylsulfamoyl-4-hydroxy-phenoxy)-1H-indole-2-carboxylic acid;
- 30 5-(3-Cyclohexylmethanesulfonyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 5-(3-Cyclopropylsulfamoyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;

- 5-(4-Hydroxy-3-isopropyl-phenoxy)-3,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 5-(4-Hydroxy-3-isopropyl-phenoxy)-1,4,6-trimethyl-1H-indole-2-carboxylic acid;
- 5 4,6-Dichloro-5-[3-(4-fluoro-benzenesulfonyl)-4-hydroxy-phenoxy]-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-[3-(4-fluoro-benzenesulfonyl-4-hydroxy-phenoxy]-3-methyl-1H-indole-2-carboxylic acid;
- 5-(3-Cyclobutylsulfamoyl-4-hydroxy-phenoxy)-4,6-dimethyl-1H-indole-2-
- 10 carboxylic acid;
- 5-[4-Hydroxy-3-(1-isopropyl-2-methyl-propylcarbamoyl)-phenoxy]-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-[3-[(4-fluoro-phenyl)-hydroxy-methyl]-4-hydroxy-phenoxy]-1H-indole-2-carboxylic acid;
- 15 5-(4-Hydroxy-2,3-dimethyl-phenoxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-(4-hydroxy-2,3-dimethyl-phenoxy)-1H-indole-2-carboxylic acid;
- 5-(7-Hydroxy-indan-4-yloxy)-4,6-dimethyl-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-(7-hydroxy-indan-4-yloxy)-1H-indole-2-carboxylic acid;
- 4,6-Dichloro-5-(4-hydroxy-5,6,7,8-tetrahydro-naphthalen-1-yloxy)-1H-indole-2-
- 20 carboxylic acid; and
- 5-(4-Hydroxy-5,6,7,8-tetrahydro-naphthalen-1-yloxy)-4,6-dimethyl-1H-indole-2-carboxylic acid.
32. A composition of claim 21, 23, 24, 26, 27, 28 or 30 wherein the topical composition is in the form of a lotion, cream, ointment, paste, lacquer, artificial nail,
- 25 gel, spray, aerosol, bandage or kit; and the effective amount of the compound is about 0.0001% to about 10% (w/v) of the compound per day.
33. A composition of claim 21, 23, 24, 26, 27, 28 or 30 which further comprises an effective amount of nail growth promoter, an antibacterial agent or an antifungal agent.
- 30 34. A composition of claim 33 wherein the antifungal agent is fluconazole, itraconazole, terbinafine or ciclopirox.
35. A kit for increasing nail growth in a mammal, the kit comprising:
- a) a first pharmaceutical composition comprising a compound of claim 4, 6, 7, 9, 10 11 or 13;

b) a second pharmaceutical composition comprising a second compound useful for promoting the rate of nail growth, an antibacterial agent or an antifungal agent; and

c) a container.

5 36. A kit of claim 35 wherein the additional compound is an antifungal agent is fluconazole, itraconazole, terbinafine or ciclopirox.

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